Crossmodal spatial representations:

Behavioural and electrophysiological evidence on the effects of vision and posture on somatosensory processing in normal population and in right-brain-damaged patients

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To my little nephew Riccardo

(to whom my sister is trying to teach the phrase 'cognitive neuroscience')

Abstract

Interactions between different sensory modalities can affect processing of unisensory information, at both a perceptual and a neural level. The studies reported in this thesis address the effects of crossmodal interactions between vision and touch on tactile processing. In particular, these studies provide new behavioural and neural (ERP; event related potentials) evidence showing that: i) crossmodal interactions enhance tactile processing when (task-irrelevant) visual stimuli are presented, simultaneously with touch, at the same location as tactile stimuli compared to a different location in near or in far space; ii) crossmodal interactions between spatial congruent visual and tactile stimuli enhance tactile processing compared to incongruent visuo-tactile stimulation, also when (task-irrelevant) visual stimuli presented near the body are observed indirectly in a mirror (i.e., appearing in far space), although in this condition these crossmodal spatial modulations are delayed compared to direct viewing of the visual stimuli; iii) vision of the body (i.e., the hands) facilitates tactile-spatial attentional selection, as compared to no visual input (blindfolded condition), and also compared to visual-spatial information only (i.e., when the hands are hidden from view); iv) in right-brain-damaged patients with tactile neglect and/or extinction, vision of the stimulated hand may further improve speed processing of contralesional tactile stimuli when the left, contralesional hand is placed in the right, 'intact' hemispace, under crossed posture.

In these studies, visual modulations of touch were present at early time intervals (i.e., early ERP components), suggesting that crossmodal spatial interactions can affect processing in cortical areas that have been considered 'modality-specific', namely, the secondary somatosensory cortex (SII). Taken together, the findings from the studies in this thesis provide new behavioural and ERP evidence in support of crossmodal spatial representations of the body and of the space surrounding the body (i.e., peripersonal space) in humans.

Overview of the thesis

In everyday life, when we interact with objects (e.g., when grasping a pencil) or other people (e.g., when shaking someone's hand), and even when we passively observe a scene happening in front of our eyes, generally more than one sense (e.g., vision, touch, hearing) is stimulated. It is certainly an interesting matter trying to understand how the physical properties of the objects (e.g., light wavelength, surface texture) are translated into sensations within just one sensory modality (e.g., vision or touch). But in recent years neuroscientists have been more and more fascinated by the challenge of comprehending how the brain can integrate the information from different senses in order to achieve a coherent phenomenological experience of our body and of the external world. Since the first pioneering studies (see, e.g., Stein, Magalhães-Castro, & Kruger, 1976), a large body of evidence has been accumulated on the fundamental principles that govern multisensory integration (e.g., spatial and temporal rules) and their underlying brain mechanisms by using a variety of methodological approaches, such as single-cell recordings, neuroimaging, neuropsychological studies, and behavioural paradigms. In addition, some of these studies have shown that integration of multimodal stimuli may also affect processing of unisensory information (see, e.g., Macaluso & Driver, 2005 for a review). Yet, many questions remain to be elucidated. Moreover, crossmodal interactions between certain sensory modalities (e.g., visual-auditory interactions, including speech perception) have received greater attention than others.

The general aim of the studies presented in this thesis was to investigate the influences of vision and posture on somatosensory processing in neurologically unimpaired people and in brain-damaged patients by means of behavioural and ERP (event-related potentials) measures. This thesis presents new findings and illustrates how these tally with previous relevant research.

In the first part of this thesis, previous evidence relevant to crossmodal spatial interactions between vision and touch will be presented from a variety of approaches (i.e., neurophysiology, neuroimaging, and neuropsychology). Particular relevance will be given to findings in support of an integrated visuo-tactile representation of peripersonal space (i.e., the space around the body; see Rizzolatti, Fadiga, Fogassi, &

Gallese, 1997) (Chapter 1). A special form of visuo-tactile interaction, namely influences of non-informative vision of the body on tactile processing, will be then described and discussed in the light of recent findings (Chapter 2). A number of outstanding questions within these research areas, which have been addressed in the experimental studies presented in this thesis, will be outlined at the end of these chapters. The second part of this thesis (Chapters 3 to 6) will illustrate how these questions have been addressed in new experiments in an attempt to gain a better understanding of the processes involved. Four studies have been conducted. The first study has investigated, by using a new paradigm, whether crossmodal visuo-tactile interactions modulate tactile processing (i.e., response times to tactile stimuli and processing within somatosensory cortex) depending on the spatial relationship between tactile stimuli and task-irrelevant visual stimuli (with the visual stimuli being presented in peripersonal and far space). This study has been published in the Journal of Cognitive Neuroscience (Chapter 3). The second study has addressed the issue of whether tactile processing may be modulated by crossmodal visuo-tactile spatial interactions when task-irrelevant visual stimuli are presented near the body and are viewed indirectly in a mirror (so that the retinal image of visual stimuli corresponds to an image generated by far objects). A paper on this study has been submitted for publication (Chapter 4). In the third study we have tested the hypothesis that visual input, and in particular the sight of the body, modulates mechanisms underlying covert sustained tactile-spatial attention. A paper on this study has been published in the European Journal of Neuroscience (Chapter 5). The fourth study has explored the influences of vision of the body on a postural manipulation (i.e., crossing the hands over the bodily midline) that in previous studies has been shown to improve tactile awareness of contralesional stimuli in right-brain-damaged patients with spatial and attentional disorders (i.e., tactile neglect and extinction); and the possible neural mechanisms underlying this 'crossed-hands' effect (Chapter 6). A paper on this study has been submitted for publication. The manuscripts presented in Chapters 3 to 6 appear as they were published or submitted, with only minor revision for consistency within this thesis. Finally, a summary of the findings from the experimental studies presented in this thesis and suggestions for future investigations will be outlined in the concluding chapter (Chapter 7).

In all studies presented in this thesis, ERPs (event-related potentials) have been recorded in addition to behavioural measures (i.e., reaction times; RTs). Thanks to the high temporal resolution of ERP measures, it has been possible to gain insights about

the time courses of the neural mechanisms underlying the processes under investigation. Temporal aspects of the brain processes that have been investigated in each study will be discussed in relation to behavioural data in each of the relevant chapters.

Chapter 1

Crossmodal spatial interactions between vision and touch

1.1 Introduction

As outlined in the Overview of the thesis, in everyday life we commonly experience 'multisensory events'; that is, events that convey information in more than one sensory modality. The complex function of the brain is to transduce the signals that are picked up by sensory receptors of different modalities and, at some point in the neural pathway, to combine these signals together to finally generate a coherent and unitary multisensory percept.

In the past few decades an increasing body of research has revealed that multisensory integration, at least for the modalities that have been studied most extensively (e.g., vision, hearing, and touch), is governed by an ensemble of *rules,* such as the rule of spatial congruence (between crossmodal stimuli) and the temporal synchronicity rule. This chapter will focus on the principle that visual and tactile events in spatial proximity produce greater crossmodal effects than bimodal stimuli that are not spatially aligned. This principle, known as spatial rule of multisensory integration, has been first demonstrated with single-cell recordings in cats (see Drager & Hubel, 1976; Meredith & Stein, 1983), and since then it has received support from other methodological approaches. Relevant evidence on spatial constraints of crossmodal interactions between vision and touch from different approaches will be reviewed below.

1.2 Neurophysiological evidence of visuo-tactile spatial integration

The spatial rule of multisensory integration was first defined in the context of neurophysiological studies in the superior colliculus (SC) of the cats' brain (Meredith & Stein, 1983; Stein, 1998; Wallace, Meredith, & Stein, 1992). A proportion of neurons in

this midbrain region (i.e., up to about 60%; Wallace & Stein, 1996) have been shown to have multisensory properties; that is, to respond to stimuli from more than one sensory modality (e.g., vision and touch). These multisensory neurons are found in deep layers of the SC, and have multiple receptive fields (RFs) (e.g., visual and tactile RFs) which are in spatial register, that is, they overlap in space. As a result, multisensory stimuli presented from the same spatial location, or more precisely within the overlapping sensory-specific receptive fields of the same neuron, sometimes produce enhanced responses in a given neuron compared to the sum of unimodal responses, and also compared to multisensory stimulation when one of the stimuli is presented outside the neuron's receptive field. The responses of these multisensory neurons can also be depressed, as when one of the stimuli falls in the inhibitory region of a neuron's receptive field. These multisensory effects (i.e., response enhancement or depression for bimodal compared to unimodal stimuli) are non-linear; that is, they do not correspond to the algebraic sum of unimodal responses (e.g., Meredith & Stein, 1983). However, linear (i.e., additive) responses have also been shown in a proportion of neurons in the SC (see Stanford & Stein, 2007); suggesting overall that multisensory processing is subserved by multiple neural mechanisms. Recent work has further characterized the spatial receptive field (SRF) architecture of multisensory neurons in the SC, revealing multiple regions of higher unimodal response (defined as "hot spots") surrounded by regions of reduced response (Carriere, Royal, & Wallace, 2008; Krueger, Royal, Fister, & Wallace, 2009). "Hot spots" for different sensory modalities may be in spatial register, although neurons showing spatial mismatch have also been found. A complex relationship between unimodal and multimodal SRFs has been shown, in that bimodal stimuli presented at an effective location for at least one modality (i.e., within a "hot spot" of the RF of a given neuron) result in additive or sub-additive responses of that particular neuron, while bimodal stimuli presented at weakly effective locations result in super-additive responses. These findings illustrate the complexity of multisensory interactions present in this sub-cortical station of integration between modalities.

Another substantial body of research in non-human primates has examined whether the principlesof multisensory integration as revealed in the SC may also apply to other brain structures, with particular interest to associative cortical areas. Neurophysiological studies, mainly in the macaque monkeys, have uncovered areas of convergence of crossmodal visuo-tactile inputs, such as the ventral intraparietal area (VIP) (Avillac, Ben Hamed, & Duhamel, 2007; Bremmer, Schlack, Duhamel, Graf, &

Fink, 2001a; Duhamel, Colby, & Goldberg, 1991, 1998; Schlack, Sterbing-D'Angel, Hartung, Hoffman, & Bremmer, 2005), the parietal area 7b (Graziano & Gross, 1995; Hyvarinen & Poranen, 1974; Leinonen, Hyvarinen, Nyman & Linnankoski, 1979; Leinonen & Nyman, 1979), and the ventral premotor area (Fogassi, Gallese, Fadiga, Luppino, Matelli, & Rizzolatti, 1996; Graziano, Hu, & Gross, 1997; Graziano, Yap, & Gross, 1994; Rizzolatti, Scandolara, Matelli, & Gentilucci, 1981). These areas contain a high proportion (up to 70%) of bimodal neurons which have spatially aligned visual and tactile RFs (see Duhamel et al., 1998; Graziano & Gross, 1993). Accordingly, the frequency of discharge of these neurons has been shown to decrease as the distance between visual stimuli and the body part touched increases. Moreover, in about 70% of bimodal neurons visual RFs are anchored to the body, and move when the body part moves in space, so that they maintain spatial alignment with the tactile RFs (Graziano, Hu, & Gross, 1997). Due to these properties, these multisensory brain areas are thought to be involved in the visuo-tactile representation of peripersonal space, that is, the space surrounding the body (Rizzolatti et al., 1997).

According to hierarchical models, multisensory integration may result from feedforward projections from sensory-specific cortical areas to heteromodal associative areas. For example, somatosensory and visual inputs are initially processed in primary sensory cortices (i.e., Brodmann's areas 3 and 1 in primary somatosensory cortex, SI, and primary visual area, V1, respectively). Somatosensory information is subsequently channelled to areas 2 and 5 (i.e., in secondary somatosensory cortex, SII), and then routed into the medial bank of the intraparietal sulcus (IPS) (Jones & Powell, 1970; Pandya & Kuypers, 1969; Seltzer & Pandya, 1986). Visual processing proceeds from secondary visual areas along the dorsal and ventral visual streams. In the intraparietal sulcus, the dorsal visual stream meets the somatosensory processing stream (Neal, Pearson, & Powell, 1990; Selzer & Pandya, 1980). Furthermore, multiple feedforward and feedback projections connect the IPS with the *polysensory zone* in the ventral premotor cortex (Lu, Preston, & Strick, 1994; Takada, Nambu, Hatanaka, Tachibana, Miyachi, et al., 2004; Tomassini, Jbabdi, Klein, Behrens, Pozzilli, et al., 2007). According to this model, top down modulations from multimodal associative areas may be responsible for crossmodal *spatial* effects observed in modality-specific areas. (see section 1.3 for more details). On the other hand, recent studies in animals have also shown direct anatomical connections between sensory-specific cortical areas, including connections between somatosensory areas (1 and 3b) and visual areas in the

inferotemporal cortex (Cappe & Barone, 2005; Falchier, Clavagnier, Barone, & Kennedy, 2002; Ghazanfar & Schroeder, 2006). These direct projections are thought to be responsible for the multisensory effects observed at early stages of processing (around 50 ms after stimuli onset) in a number of ERP studies (Foxe, Wylie, Martinez, Schroeder, Javitt, et al., 2002; Giard & Peronnet, 1999; Murray, Molholm, Michel, Heslenfeld, Ritter, et al., 2004). Indeed, such early latencies of multisensory interactions rule out a role for top-down modulations from polymodal associative areas. In addition, because in the abovementioned studies multisensory effects were found to be present irrespective of the relative spatial position of multimodal stimuli, it has been suggested that direct pathways between modality-specific areas may operate in a non-spatially specific manner, possibly fulfilling an arousal function (see Macaluso & Driver, 2005).

In conclusion, neurophysiological studies in animals have provided significant evidence on the neural mechanisms involved in multisensory processing. These findings have stimulated a number of studies to investigate whether similar mechanisms and principles of multimodal integration are also found in humans. These studies will be reviewed in the following sections.

1.3 Evidence of visuo-tactile spatial interactions from neuroimaging studies in humans

While neurophysiological recording studies in animals have investigated mechanisms of multisensory integration at the level of single neurons, neuroimaging research has aimed to seek the neural correlates of multisensory integration in humans at the whole-brain level. In the past decade, functional magnetic resonance imaging (fMRI) and positron emission tomography (PET) techniques have been increasingly used to identify the brain regions involved in multisensory integration, and in addition to investigate to what extent the principles and properties of multisensory integration (e.g., spatial rule) measured at the single-neuron level in animals can also be revealed in the human brain. Bremmer and colleagues (Bremmer, Schlack, Shah, Zafiris, Kubischik et al., 2001b) were among the first to compare brain responses (fMRI activation signals) to stimuli in individual sensory modalities (i.e., visual, auditory, and somatosensory) presented one at a time, in order to identify regions showing common activity, that is, areas that are activated by more than one or all these modalities. Using this paradigm,

these authors were able to identify a network of candidate multisensory areas, including the intraparietal sulcus (IPS), the ventral premotor cortex, and the lateral inferior postcentral cortex, closely matching the findings on multimodal integration in animals (see above). Other neuroimaging studies have looked at the neural substrates of multisensory processing by presenting multimodal stimuli, e.g., visual and tactile, synchronously. For example, in a PET study Macaluso, Frith, & Driver (2002a) have demonstrated crossmodal links in spatial attention between vision and touch in multimodal areas (i.e., intraparietal sulcus, IPS) as well as in modality-specific areas (i.e., visual cortex). These authors found that attending to one side of space (i.e., sustained attention) within one sensory modality (i.e., either vision or touch) during bilateral, bimodal visuo-tactile stimulation produced enhanced brain responses for stimuli presented at attended compared unattended locations in these brain regions, independently of the modality attended.

Of more interest to this thesis, in a series of studies, Macaluso and colleagues (Macaluso & Driver, 2001; Macaluso, Frith, & Driver, 2000a, 2001, 2002b, 2005; see also Macaluso, 2006 and Macaluso & Driver, 2005 for reviews) have examined fMRI brain activations for vision and touch to investigate the role of spatial relationships between visual and tactile stimuli in modulating responses to multisensory inputs. These authors compared haemodynamic responses to bimodal visuo-tactile stimuli with the responses obtained when stimuli of one modality (i.e., vision or touch, in separate experiments) were presented alone. In the bimodal condition the relative spatial location of visual and tactile stimuli was manipulated so that bimodal stimuli could be spatially aligned or not. Crucially, stronger activations were observed for bimodal than unimodal stimulations specifically when visual and tactile stimuli were spatially congruent. Interestingly, this modulation was found in modality-specific areas (i.e., visual cortex and parietal operculum, the latter corresponding to secondary somatosensory area), suggesting that activity in cortical areas largely assumed to be 'unimodal' can be modulated by interactions between stimuli in different modalities. On the basis of recent electrophysiological studies in animals and humans (Eimer, 2004; Falchier et al., 2002; Zhou & Fuster, 2000), which have provided new evidence on the temporal dynamics of multisensory neural processing, Macaluso and Driver (2005) argue that these spatially-specific crossmodal effects in 'unimodal' areas may result from top-down modulations from polisensory areas (i.e., intraparietal sulcus and ventral premotor cortex) via feedback projections.

In sum, neuroimaging techniques have revealed a network of human brain areas involved in crossmodal spatial interactions between vision and touch. However, in these studies visual stimuli were always presented near the body, and therefore no comparisons were made between conditions in which visual stimuli are presented in near and far space. Thus, from these studies it is not possible to conclude whether these brain regions are specifically involved in the visuo-tactile representation of peripersonal space in humans; that is, whether they follow the spatial rule of multisensory integration as shown by neurophysiological studies. More recently, one fMRI study (Makin, Holmes, & Zohary, 2007) has compared responses to visual stimuli presented in near and far space, and found greater activations for near compared to far visual stimuli in the intraparietal sulcus (IPS, a multimodal cortical region; see above) and in some regions of the lateral occipital complex (LOC). However, in this study tactile stimuli were not presented simultaneously with visual stimuli. Crucially, Makin et al. found that the 'preference' for near compared to far visual stimuli shown by the abovementioned areas was modulated by the distance of the visual stimuli from the participants' body parts (i.e., the hand), and by whether visual information about the participants' own hand (or a dummy hand) was available or not. They found that the posterior IPS and some regions within the LOC were more activated when the participants' hand (or a dummy hand) was *visible* next to the (near) visual stimuli, regardless of the actual position of the participants' hand (i.e., being either next to the visual stimuli or retracted away, in different conditions). This suggests visual dominance over proprioception in the representation of peri-hand space in these areas. On the other hand, the anterior IPS was more sensitive to the *position* of the participants' hand with respect to the visual stimuli, showing greater activation when the participants' own hand was positioned next to the visual stimuli but occluded from view compared to when a dummy hand was visible next to the visual stimuli while the participants' hand was retracted away. Taken together, these results indicate that these areas may be involved in representing nearby visual space with respect to the hand (i.e., peri-hand space) with a selective preference for visual or proprioceptive information regarding the hand.

1.4 Visuo-tactile spatial effects in behavioural studies

Spatial modulations of visual-tactile interactions have also been shown at a behavioural level. Early behavioural studies focussed on crossmodal links in endogenous and exogenous spatial attention between vision and touch, with visual and tactile stimuli not being presented simultaneously (Butter, Buchtel, & Santucci, 1989; Kennett, Spence, & Driver, 2002; Spence, Nicholls, Gillespie, & Driver, 1998; Spence, Pavani & Driver, 2000). For example, some of these studies found that directing attention to one side of space within one sensory modality ('primary' modality, e.g., vision) resulted in shorter response latencies also for targets in the 'secondary' modality (e.g., touch), despite the fact that stimuli in the less frequent modality were more likely to appear on the opposite side of space (Spence et al., 2000). Similarly, spatially non-predictive (exogenous) cues in one modality (e.g., vision or audition) have been shown to facilitate speeded responses to subsequent targets in a different modality (e.g., touch) when the latter were presented at the 'cued' location compared to a different location (Spence et al., 1998).

While these studies have explored spatial properties of crossmodal attention with stimuli in different modalities presented asynchronously, other behavioural studies have investigated crossmodal spatial effects when visual and tactile stimuli are concurrently presented, for example using the crossmodal congruency paradigm (e.g., Shore, Barnes, & Spence, 2006; Spence, Pavani, & Driver, 2004a; Spence, Pavani, Maravita, & Holmes, 2004b). In these studies, participants were required to judge the elevation of vibrotactile stimuli (upper, at the index finger, vs. lower, at the thumb) delivered to either hand, while trying to ignore task-irrelevant visual stimuli presented near the hands at congruent or incongruent elevations to touch. These studies found that spatial judgments of tactile stimuli were slower and less accurate when a concurrent distractor light was presented at incongruent (e.g., upper light with a lower touch), compared to congruent, elevations. Importantly, these interference effects were modulated by the distance of the visual distractors from the site of tactile stimulation, with larger crossmodal interference effects obtained when the visual distractors were presented at the same hand as the tactile targets (Spence et al., 2004a). These results suggest that task-irrelevant visual stimuli can influence tactile spatial localization, particularly when visual and tactile stimuli are presented in close spatial proximity. However, since crossmodal interference effects were dramatically reduced when participants performed

the crossmodal congruency task under unspeeded conditions, i.e. when they were asked to respond as accurately as possible (Spence et al., 2004a), this suggests that early perceptual interactions between vision and touch may not play a major role in these effects. Instead, these interferences might occur at a post-perceptual stage, and may be explained at least in part in terms of competition between response representations activated by tactile stimuli and task-irrelevant visual stimuli. That is, when visual and tactile stimuli are presented at locations that activate opposite responses (i.e., upper vs. lower elevations), response conflict would impair performance (i.e., response conflict account) (Shore & Simic, 2005; Shore et al., 2006; see also Forster & Pavone, 2008 for electrophysiological support of this account).

Of particular relevance for this thesis (see Chapter 4), one study using the crossmodal congruency task found that crossmodal interferences of visual distractors on tactile elevation judgments were more effective when the visual distractors presented near the hands were observed via a mirror compared to conditions in which these were presented in a region of the space out-of-reaching (i.e., far extra-personal space; Maravita, Spence, Sergent, & Driver, 2002a) at a distance that produced a comparable visual image as the mirror image. However, no previous behavioural studies have directly compared conditions in which visual distractors are presented, and directly observed, near the hands and in far space.

1.5 Neuropsychological evidence of near-far visuo-tactile modulations

Until about a decade ago, neuropsychological studies were investigating perceptual and cognitive functions (e.g., sensory awareness, attention) in brain-damaged patients by using one single modality at a time. For example, a great amount of research has shown that right-brain-damaged patients may exhibit perceptual neglect and/or extinction for, e.g., visual or tactile stimuli (Bender, 1952; Heilman, Bowers, Valenstein, & Watson, 1993; Moscovitch & Behrmann, 1994). That is, these patients may not report visual or tactile stimuli on the contralesional side of space when presented either in isolation (visual or tactile neglect) or simultaneously with an ipsilesional stimulus in the same modality (visual or tactile extinction). These deficits have been attributed to spatial and/or attentional disorders (see e.g., Bottini, Paulesu, Gandola, Loffredo, Scarpa, et al., 2005; Vallar, 1998). Since pioneering neurophysiological studies have revealed multisensory properties of cortical areas that

are also involved in attentional and spatial processing (i.e., fronto-parietal areas; see above), a number of neuropsychological studies have sought to investigate whether perceptual deficits exhibited by right-brain-damaged patients (i.e., neglect and extinction) in one modality may be modulated by the presentation of stimuli in a different modality. For instance, a series of studies (di Pellegrino, Làdavas, & Farnè, 1997; Làdavas, di Pellegrino, Farnè, & Zeloni, 1998; Làdavas, Farnè, Zeloni, & di Pellegrino, 2000; see Làdavas & Farnè, 2004a, 2004b for reviews of these studies) have reported that a task-irrelevant visual stimulus presented near the patients' ipsilateral hand can extinguish a contralesional tactile stimulus delivered simultaneously (*crossmodal extinction*), in a similar way as an ipsilesional tactile stimulus does. Moreover, it has been shown that detection of contralesional tactile stimuli can be improved by a task-irrelevant visual stimulus presented near the patients' contralesional hand simultaneously with double (left and right) tactile stimulation (*crossmodal modulation of tactile extinction*) (Làdavas et al., 1998; see Làdavas, 2002 for a review). Crucially, both these crossmodal effects have been shown to be modulated by the spatial distance of visual stimuli from the body. Namely, visual modulations of touch have been reported when visual stimuli are presented near the hands, while these crossmodal effects are dramatically reduced when visual stimuli are moved away from the body in far space (i.e., at a distance of ~ 35 cm from the hands) (Làdavas, 2002; Làdavas et al., 1998), in accordance with the evidence from animal studies that bimodal neurons decrease their firing when the distance between visual stimuli and the body increases (see, e.g., Duhamel et al., 1991). Taken together, these findings in brain-damaged patients are in line with neurophysiological evidence of multisensory integration, and suggest that, similarly to what has been shown in animals, a network of brain regions mainly including frontal and parietal areas may be responsible for crossmodal representation of peripersonal space. Interestingly, recent evidence in right-brain-damaged patients, as well as in neurologically unimpaired people, has shown that visuo-tactile representation of peripersonal space is plastic and can incorporate regions of extra-personal space that become reachable by means of tools, and regions of space near the body that are 'projected' in far space via a mirror (Farnè, Iriki, & Làdavas, 2005; Pavani, Spence, & Driver, 2000; Maravita, Clarke, Husain, & Driver, 2002; Maravita, Husain, Clarke & Driver; 2001; Maravita, Spence, Sergent, & Driver, 2002b). This evidence will be further discussed in Chapter 4.

1.6 ERP investigations on the 'spatial rule' of visuo-tactile integration

Event-related potentials (ERP) and magnetoencephalography (MEG) are the most suited techniques to investigate the time course of crossmodal integration in humans. Surprisingly, however, only a limited amount of research has investigated crossmodal interactions between vision and touch using these techniques. A number of studies have reported crossmodal links between vision and touch in covert spatial attention (Eimer, 2001; Eimer, Cockburn, Smedley, & Driver, 2001; Eimer & Driver, 2000; Kennett, Eimer, Spence, & Driver, 2001a). For instance, some of these studies (Eimer & Driver, 2000; Eimer et al., 2001) found that attending to a certain spatial location in order to respond to, e.g., tactile target stimuli at that location, not only enhanced somatosensory ERPs in response to tactile stimuli at attended compared to unattended locations, but also modulated early visual ERPs elicited by infrequent, task-irrelevant visual stimuli, with enhanced amplitudes for visual stimuli presented at tactually attended, compared to unattended, locations[1]. Likewise, ERPs in response to target stimuli in one modality (e.g., vision) have been shown to be affected by spatially non-predictive (exogenous) cues in a different modality (e.g., touch), with enhanced ERPs for targets presented at the location where attention was exogenously directed compared to a different location (Kennett et al., 2001a). Taken together, these findings support at least partially the hypothesis of a supra-modal attentional system governed by a spatial congruence rule (see Eimer et al., 2001 for a detailed discussion of this account).

However, as in the ERP studies outlined above visual and tactile stimuli were not concurrently presented, from these studies no specific conclusions can be drawn upon spatial properties of visuo-tactile integration. To the best of our knowledge, only two ERP studies have investigated spatial constraints of visuo-tactile integration when visual and tactile stimuli are presented simultaneously (Piesco, Molholm, Sehatpour, Ritter, & Foxe, 2005; Schürmann, Kolev, Menzel, & Yordanova, 2002). These studies have sought to identify ERP correlates of the spatial principle of multisensory integration between vision and touch in humans corresponding to the 'spatial rule' revealed by single-unit recordings in animals. For this purpose, these studies have adopted a method similar to that used by neurophysiological studies in animals. That is, ERPs obtained in

[1] By contrast, when vision was the primary (i.e., task-relevant) modality while tactile stimuli had to be entirely ignored, no attentional modulations of somatosensory ERPs in response to infrequent tactile stimuli were obtained, suggesting that touch may be decoupled from visual-spatial attention when it is entirely task-irrelevant.

response to simultaneous bimodal stimulation are compared with the algebraic sum of ERPs elicited by unimodal single stimuli. Differences between ERP in response to bimodal stimulation and the sum of unimodal responses are regarded as effects of multisensory integration (i.e., super-additive or sub-additive effects depending on the sign, positive or negative respectively, of these differences). As appealing as this method may appear to draw parallels between animal and human multisensory research, theoretical and methodological limitations of this approach have been recently pointed out (see Gondan & Röder, 2006; Stanford & Stein, 2007; Teder-Sälejärvi, McDonald, Di Russo, & Hillyard, 2002). For example, as Stanford and Stein (2007) maintain, one consequence of using this method is a disproportionate emphasis given to non-linear (super- and sub-additive) multisensory responses over 'additional' responses in accounting for crossmodal integration mechanisms. As these authors have pointed out, non-linear single-cell responses seem to be constrained to weak multimodal stimuli and are especially found, although not only, in neurons of the superior colliculus (SC); which suggests that non-linearity is a context-specific mechanism within the spectrum of multisensory processing. From a methodological point of view, it has been argued that using this subtractive method (i.e., subtraction of the sum of unimodal from bimodal responses; e.g., VA – (V+A), where V stands for visual and A for auditory[2]) may produce distortions in the ERP data, especially at early time windows. Distortions would arise because common activity (C) unrelated to multisensory processing (e.g., stimulus expectation or motor preparation activity) is subtracted twice from the bimodal ERPs (i.e., AVC – [AC+VC] → AVC – 2C [A+V]), which as a result alters the ERP waveforms. Gondan and Röder (2006) have recently proposed a new approach to assess super- and sub-additive effects in audio-visual interactions in ERPs, which requires coupling of a tactile (T) stimulus to each unimodal (auditory or visual) and bimodal (audio-visual) stimulus presentation (i.e., AT, VT, and AVT), and the inclusion of a number of unimodal tactile trials. This method consists in subtracting two ERPs from two others as follows: (AVT + T) – (AT + VT). As a result, common activity as well as unimodal ERP activity may be eliminated, because this activity is present in equal proportion in the two terms of the subtraction. In addition, activity arising from interactions of the auditory and the tactile system, and the visual and the tactile system should also be eliminated in the subtraction because this is also present in both terms of

[2] Examples are given for audio-visual integration for consistency reasons, as this critique has been first raised in the context of audio-visual interactions.

the subtraction. Finally, trimodal interactions might be also present in the ERPs elicited by audio-visuo-tactile stimuli, and this activity can be isolated in the comparison, together with the relevant audio-visual interactions. With this new method, Gondan and Röder (2006) found that the earliest indication of audio-visual interaction in ERPs was around 80 ms after stimulus onset; that is, about 30-40 ms later than previous findings obtained by using the algebraic method described above without correcting for common activity.

In principle, this new method could be used also to assess visuo-tactile interactions. In practice, however, the complexity of the design would make it difficult, if not impossible, to explore the role of spatial relationships between multisensory stimuli. Indeed, the addition of an auditory stimulus to the bimodal visuo-tactile stimuli would require controlling for the spatial location of the former relative to the location of the visual and tactile stimuli. Moreover, the auditory stimulus could potentially drive exogenous attention towards the spatial location where this is presented.

The two ERP studies mentioned above (Piesco et al., 2005; Schürmann et al., 2002) that have examined spatial constraints of visuo-tactile interactions, have, however, used bimodal (not trimodal) stimuli, and therefore are not immune from the criticism described above. In addition, the findings from these two studies suggest somewhat different conclusions on the role of spatial congruence between bimodal stimuli in visuo-tactile interactions. In particular, in one of these studies (Piesco et al., 2005) bimodal interaction effects (i.e., differences between ERPs in response to bimodal stimulation compared to the sum of unimodal responses) were found to be present regardless of spatial congruence between visual and tactile stimuli. In the other study (Schürmann et al., 2002), bimodal interaction effects were found to occur regardless of the relative location of the visual stimuli at some electrode sites, while at other sites bimodal effects were only obtained when visual stimuli were presented in the same (congruent), compared to the opposite (incongruent), hemispace as tactile stimuli. These two ERP studies also differ about the distance at which visual stimuli were presented from the body; that is, in Piesco et al.'s study visual stimuli were presented near the body (i.e., in peri-hand space), while in the study by Schürmann and colleagues visual stimuli were presented at a distance of one metre from the participants' body (i.e., in extra-personal space). Crucially, none of these two studies have directly addressed the issue of whether crossmodal interactions between vision and touch are modulated by the distance of visual stimuli from the body (i.e., in peripersonal space vs. far space).

Finally, it is worth noting that in the ERP studies described above participants were either performing a simple detection task (Piesco et al., 2005) or were not engaged in any task (Schürmann et al., 2002); and, in particular, the spatial location of stimuli was not relevant to the task in either study. Importantly, it has been argued that spatial effects in multisensory paradigms are less likely to be present in low complexity tasks (Forster, Cavina-Pratesi, Aglioti, & Berlucchi, 2002; Gondan, Niederhaus, Rosler, & Röder, 2005; Posner, 1978). Namely, when spatial location of stimuli is not relevant to the task as in simple detection tasks, processing of spatial information concerning sensory stimuli may be limited, and crossmodal interactions may occur regardless of spatial congruence between multisensory stimuli, possibly by direct connections between modality-specific areas as suggested by previous models (see Eimer & Driver, 2000; Eimer et al., 2001; Macaluso & Driver, 2005). In sum, the ERP findings discussed above are inconclusive on whether visuo-tactile integration requires or not spatial congruence between multisensory stimuli. In addition, no ERP study has hitherto compared responses to bimodal visuo-tactile stimuli when visual stimuli are presented in peripersonal space near the hands (i.e., peri-hand space) and at a distance from the body in far space.

1.7 Attentional modulations of crossmodal spatial interactions

In the context of studies on multisensory integration, a further interesting issue is to establish whether signals from different modalities are integrated pre-attentively or whether attention modulates crossmodal interactions. In the literature of multisensory interactions there are findings in support of both hypotheses, suggesting that the relationship between crossmodal interactions and attention may vary depending on experimental factors. Some of these studies have manipulated the attentional load in bimodal task conditions, or whether attention is directed to one or the other modality, without manipulating the spatial distribution of attention. For instance, in the visuo-tactile domain Helbig and Ernst (2008) found that when attention was withdrawn from vision by using a distractor task that consisted of same/different judgments of rapidly presented visual letter sequences, participants were still able to integrate visual and haptic size information of a target stimulus (bar) in a dual-task condition. These authors conclude that because reducing modality specific (i.e., visual) attention does not influence the performance in the 'bimodal task' condition (which was always better than

in the 'unimodal' task conditions), multisensory integration must take place automatically at a pre-attentive level of processing. On the other hand, because in the study by Helbig and Ernst the visual sequences of letters appeared at the same spatial location as the target bar in order to keep spatial attention constant throughout the task, from this study no conclusions can be made on whether visuo-tactile integration may be affected by the focus of spatial attention; namely, by whether attention is directed or not to the site of visual and tactile stimuli.

More directly related to the purpose of the present thesis are the effects of *spatial* attention on crossmodal interactions, which have been predominantly investigated within the audio-visual domain. Evidence in support of the automatic, pre-attentive nature of multisensory integration comes from studies that have manipulated spatial attention to the location of sensory inputs in one of the two modalities (e.g., Bertelson, Vroomen, De Gelder, & Driver, 2000; Vroomen, Bertelson, & de Gelder, 2001). For example, behavioural studies on the ventriloquist effect (Bertelson et al., 2000; Vroomen et al., 2001) have shown that mislocalisation of sounds towards visual locations is largely unaffected by manipulations of visual spatial attention. In addition, a number of ERP studies have shown that audio-visual interactions may take place relatively early in the processing stream (i.e., around 50 ms after stimuli onset), suggesting that multisensory integration may not require conscious processing (Foxe, Morocz, Murray, Higgings, Javitt, & Schroeder, 2000; Giard & Peronnet, 1999; Molholm, Ritter, Murray, Javitt, Schroeder, & Foxe, 2002). In contrast, there is also ERP evidence suggesting that multisensory integration and attention may interact. For instance, Talsma and Woldorff (2005) found that audio-visual integration effects on ERPs (i.e., super-additive responses) were larger in amplitude and occurred earlier (i.e., about 100 ms after stimuli onset) when attention was directed to the (peripheral) site where visual and auditory stimuli were presented; and in a subsequent study Talsma, Doty, and Woldorff (2007) showed that early super-additive effects (i.e., about 50 ms after stimuli onset) for centrally presented stimuli at attended, compared to unattended, locations depended specifically on both visual and auditory modalities being attended.

In sum, findings on the interplay between multisensory integration and attention are inconclusive. On the other hand, it is possible to hypothesize that the discrepancies in the findings from the studies above (including the different time courses of the effects in the ERP studies by Talsma & Woldorff, 2005, and Talsma et al., 2007), may be due to differences in the experimental procedures, such as in the attentional manipulations

used, in the location of stimulus presentation, and whether one or both sensory modalities were attended. As will be explained in the next section (1.8), in the studies reported in Chapters 3 and 4 tactile-spatial attention was manipulated with the main purpose of making spatial location relevant to the task (see above, Gondan et al., 2005). In addition, this attentional manipulation has given us the opportunity to explore the effects of tactile-spatial attention on visuo-tactile spatial interactions on ERPs, an issue that has not been addressed in previous studies.

1.8 Outstanding questions and novelty of the paradigm used in the studies in this thesis

To summarize the findings from previous studies described in this chapter: there is a growing body of evidence showing that visuo-tactile interactions are modulated by spatial congruence between visual and tactile stimuli. These spatial-congruence effects were first shown in neurophysiological studies (which have established the so-called 'spatial rule' of multisensory integration) and have received support from fMRI and neuropsychological studies, while findings from previous ERP studies are inconclusive. Moreover, evidence from single-unit recordings in animals and lesions studies in humans has shown that visuo-tactile interaction effects are specifically obtained when visual stimuli are presented in proximity to the body (as compared to far space), suggesting that some multisensory brain areas may be specifically dedicated to representation of visuo-tactile peripersonal space. In contrast, to date no previous ERP or functional neuroimaging studies have compared crossmodal visuo-tactile responses under conditions in which visual stimuli are presented in peripersonal space and at a distance from the body in far space.

Furthermore, a number of behavioural studies have shown that representation of visuo-tactile peripersonal space is dynamic and may adapt to incorporate regions beyond the space surrounding the body, that is, in far space (e.g., mirror projections, the tip of a tool). These findings are fascinating and suggest that neural representations of space are 'plastic' and the brain can promptly respond in the most adaptive way to specific situations. However, these issues have not been previously addressed by neuroimaging studies, and therefore the neural mechanisms underlying plasticity of visuo-tactile peripersonal space representations were unexplored.

From a methodological point of view, the only two ERP studies that have explored spatial effects in visuo-tactile interactions have compared ERPs in response to bimodal stimuli to the algebraic sum of ERPs elicited by unimodal (visual and tactile) stimuli. This method has received some criticism, as discussed in section 1.6 of this chapter. In an attempt to overcome these limitations, we have designed a new experimental paradigm that we have used to investigate crossmodal spatial interactions between vision and touch. The novelty and the main advantages of this paradigm are described as follows. Firstly, and differently from previous studies that focussed on non-linear responses (see Piesco et al., 2005; Schürmann et al., 2002), bimodal visuo-tactile stimuli are presented in every trial (with the visual stimuli being task-irrelevant), and only the location of visual stimuli is varied in different trials. As a result, bimodal ERPs are always compared to other bimodal ERPs, (i.e., never to the sum of unimodal ERPs, see above). This paradigm allows us to specifically investigate whether the relative spatial location of task-irrelevant visual stimuli in relation to the site of tactile stimulation may modulate behavioural and electrophysiological responses associated with processing within somatosensory cortex (i.e., ERPs recorded over and close to somatosensory cortex), under the assumption that any differences between bimodal ERPs in different experimental conditions are to be attributed to the different spatial relationship between visual and tactile stimuli. Secondly, spatial location of tactile target stimuli is purposely made task-relevant under the hypothesis that crossmodal *spatial* effects are more likely to be present in spatial tasks (see section 1.6). This is obtained by manipulating sustained tactile-spatial attention; namely, participants' task is to attend to either their right or left hand throughout a block in order to detect tactile target stimuli (stimulation with a 'gap') among non-targets (continuous stimulation) at the currently attended hand. As will be described in further details, we have used this paradigm to investigate crossmodal spatial interactions between vision and touch when task-irrelevant visual stimuli are presented in peripersonal and in far space (in separate blocks of trials) (Chapter 3), and in addition to explore crossmodal spatial interactions between tactile stimuli and mirror-reflected, task-irrelevant visual stimuli (Chapter 4). One limitation of this paradigm could be that because the presentation of visual stimuli in near- versus far- versus 'mirror-' space is blocked[3] (and thus predictable in the radial

[3] Since 'mirror' visual stimuli had to be presented in separate blocks of trials for practical reason, it was chosen to also have 'near-' and 'far-space' visual stimuli in separate blocks to allow comparisons between different experimental conditions.

dimension of space), visual stimuli observed in far (and 'mirror') space might cause *divided* attention between near and far space; in contrast, attention would be *focused* within near space in 'near-space' blocks. As a result, differences in the distribution of spatial attention, rather than multisensory integration effects alone, would be at least in part responsible for the effects observed on tactile processing. This same potential confound is present in previous studies that manipulated the location of visual stimuli in near and far space (see, e.g., Ladavas et al., 1998). However, unlike these previous studies, the paradigm used in the studies presented in Chapters 3 and 4 of this thesis allows us to control for this potential confound by comparing attentional modulations of ERPs obtained under conditions when visual stimuli are presented in near-, far-, and 'mirror-' space, and rule out the possibility that crossmodal spatial effects are only accounted for by the distribution of spatial attention.

Chapter 2

Modulations of tactile processing and of tactile-spatial attention by non-informative vision of the body

2.1 Visual modulations of touch

In the previous chapter, I presented earlier findings on crossmodal spatial interactions between vision and touch. I will now turn to review recent evidence showing that non-informative vision of the body modulates (i.e., enhances) tactile processing. This effect, dubbed visual enhancement of touch (VET), is also regarded as a form of crossmodal interaction, although with special properties as it will be illustrated in this chapter.

The first demonstration that viewing the body affects tactile perception was reported about a decade ago (Tipper, Lloyd, Shorland, Dancer, Howard, & McGlone, 1998). Tipper and colleagues showed that seeing a given body part in a video monitor (e.g., the right hand) while tactile stimuli are applied to this body part speeds up tactile detection in healthy participants. Namely, reaction times (RTs) to tactile stimuli were faster when participants were shown the same body site that was being stimulated, e.g., the the right hand, compared to the opposite hand. Earlier studies reported that orienting the eyes or the head towards a body location facilitates tactile perception (Honoré, Bourdeaud'hoi, & Sparrow, 1988; Driver & Grossenbacher, 1996). Notably, in the study by Tipper et al. (1998) visual input and proprioceptive orienting were dissociated as the participants' gaze was always directed to the monitor in front of them, that is, away from the stimulated body part. Therefore, these authors suggest that vision of the body specifically improves tactile perception irrespective of proprioceptive orienting. In a follow-up study, Tipper and colleagues (Tipper, Phillips, Dancer, Lloyd, Howard, & McGlone, 2001) have further demonstrated that visual information concerning the body (presented via a video monitor) improves tactile detection also at body sites that cannot be directly viewed, such as the face. Importantly, while the results from the first of the two studies by Tipper et al. (1998) could be explained by an increase of attention towards the viewed body part (i.e., attentional cueing), in the second study (Tipper et al., 2001) this potential confound was controlled for by asking the participants to

maintain their attention to one body site throughout a block (i.e, sustained attention) and to respond to tactile stimuli at the attended site while ignoring tactile stimuli presented at different body sites. Furthermore, it was stressed to the participants that visual images of body parts did not predict target locations. Therefore, these authors argue that visual enhancement of touch found in their studies is not simply due to spatial attention, but it is a truly multisensory effect. Further studies have shown that non-informative vision of the body improves tactile spatial resolution. Kennett, Taylor-Clarke, and Haggard (2001b) have provided the first psychophysical evidence that tactile two-point discrimination thresholds (2PDT) can be improved by seeing, compared to not seeing, one's own arm, and also compared to viewing a neutral object placed at the same spatial location as the participants' arm. Moreover, a magnified view of the participants' arm further improved tactile spatial resolution, with lower tactile discrimination thresholds compared to conditions of normal visibility of the arm. This enhancement of tactile perception cannot be attributed to spatial orienting, as both tactile and visual attention was directed to the same spatial location across all viewing conditions. Rather, this effect appears to be specifically triggered by viewing one's own body.

Other studies have investigated the neural mechanisms underlying VET (Fiorio & Haggard, 2005; Taylor-Clarke, Kennett, & Haggard, 2002). One study has shown that viewing the relevant body part (i.e., the arm) during tactile stimulation modulates early somatosensory processing (Taylor-Clarke et al., 2002). Two somatosensory ERP (Event-Related Potentials) components, the N80, which is thought to originate in SI (see Hari, Reinikainen, Kaukoranta, Hämäläinen, Ilmoniemi, et al., 1984), and the N140, arising in SII (Frot & Mauguière, 1999; Hari et al., 1984), were enhanced when participants viewed their own arm compared to a neutral object placed at corresponding locations. This visual modulation of activity in early somatosensory areas has been attributed to back projections from multisensory areas such as the posterior parietal cortex to the somatosensory cortex. A more recent study has used transcranial magnetic stimulation (TMS) to clarify and localize the brain mechanisms of the VET effect (Fiorio & Haggard, 2005). Participants in this study first observed the relevant body parts (i.e., the hands), or a neutral object at the same spatial location, and were then required to discriminate the orientation of tactile gratings presented to their hands after a darkness period of two seconds. The main finding of this study (Fiorio & Haggard, 2005) is that visual enhancement of touch was abolished when TMS was applied to primary somatosensory cortex (SI), immediately after (i.e., 20 ms) tactile stimuli were

delivered, but not when TMS was applied to secondary somatosensory cortex (SII). As TMS temporarily disrupts activity of the brain areas over which it is applied, this finding suggests that SI, but not SII, is accountable for VET. SI may receive descending signals from multimodal areas of the parietal cortex that 'pre-activate' this area during vision of the body, and facilitate subsequent tactile processing (Fiorio & Haggard, 2005). Importantly, the findings from the study by Fiorio and Haggard indicate that a brain area that has been largely considered to be unimodal (SI) may be involved in crossmodal interaction effects, such as VET, via feedback projections from higher-order areas.

Taken together, the studies reported above suggest that viewing the body enhances somatosensory processing, and more specifically improves spatial resolution of touch (see also Press, Taylor-Clarke, Kennett, & Haggard, 2004). Recent studies (see Harris, Arabzadeh, Moore, & Clifford, 2007; Johnson, Burton, & Ro, 2006; see also Haggard, Christakou & Serino, 2007) have challenged and extended these assumptions, suggesting that visual enhancement of touch may not be limited to the perception of spatial attributes of tactile stimuli; and, additionally, that non-informative vision may modulate tactile processing not via a general enhancement of somatosensory responses but through *changes* in tactile sensitivity (i.e., gain control) and in response criteria. For instance, Harris et al. (2007) have shown that viewing the stimulated body part improves discrimination of supra-threshold vibro-tactile stimuli, while it impairs detection and amplitude discrimination of near-threshold tactile vibrations. In this study, similar results (i.e., an improvement of discrimination of supra-threshold tactile stimuli at the expenses of near-threshold tactile stimuli) were also found within the tactile modality only (i.e., in absence of the sight of the stimulated body part), and were accounted for by changes in tactile sensitivity. These changes in sensory gain are a property of sensory systems (e.g., visual and tactile) and are regarded as adaptive and continuous adjustments to the sensory environment (Clifford, 2002; Wainwright, 1999). Namely, such a mechanism optimizes the range of sensitivity of a sensory system around an adapting sensory stimulation (i.e., differential sensitivity), at the expenses of absolute sensitivity. These adaptive shifts would account for the selective improvement in discrimination of supra-threshold tactile stimuli as well as for the detrimental effects on processing of near-threshold tactile stimuli obtained in Harris et al.'s study. The novel finding by Harris and colleagues is that non-informative vision of the stimulated body part produces effects similar to those obtained within the tactile modality alone. In

particular, Harris et al. suggest that, as a result of an integrated visuo-tactile system which is activated by both visual and tactile inputs, adaptive shifts in tactile sensitivity may be induced not only by tactile events but also by visual ones, such as the vision of the body, possibly in an additive fashion. The findings from this study also suggest that modulations of touch produced by non-informative vision of the body are not explained by a general facilitation of somatosensory processing. This account tallies with a previous study that has shown that VET is greater in difficult spatial (tactile) discrimination tasks than in easier non-spatial tasks, suggesting that this effect is not due to a generic improvement of tactile perception (Press et al., 2004). In addition, shifts in control gain may also be responsible for reducing the receptive fields' size of somatosensory neurons, which would account for the enhancement of tactile spatial resolution found in previous studies (Harris et al., 2007; see also Haggard et al., 2007 for a similar account on visual modulations of tactile receptive fields). In sum, changes in tactile sensitivity, rather than general enhancement of somatosensory processing, are proposed to be the underlying mechanism of these visual modulations of touch by these authors (Harris et al., 2007).

Another study (Johnson et al., 2006) has claimed that non-informative vision can cause changes in response criteria for reporting touch. This study found that visual stimuli presented next to the stimulated body part (which was visible to the participants) induced response biases in reporting near-threshold tactile stimuli along with small changes in tactile sensitivity (as measured by using signal detection procedures). These authors speculate that previous findings that have shown facilitation of tactile processing by non-informative vision, including vision of the stimulated body parts, may be accounted for, at least in part, by criterion shifts. However, if this was the case we would expect visual modulations of tactile responses to be present at later, post-perceptual stages of processing and not to affect early somatosensory ERP components as reported by previous studies (see Taylor-Clarke et al., 2002).

Further indications of the modulatory role of vision of the body on tactile perception come from the neuropsychological literature. For example, Halligan, Marshall, Hunt, and Wade (1997) have reported the case of one right-brain-damaged patient who was able to detect tactile stimuli applied to his left, contralesional hand when he was allowed to see his hand, while he failed to report all the left-sided stimuli in absence of visual input. In addition, when he was shown a previously recorded video of his own hand being touched, he reported tactile stimuli even in absence of any

stimulation (i.e., false alarms), in line with the view that vision of the stimulated body part may also induce shifts in the response criterion (Johnson et al., 2006).

By using a more controlled experimental design, Rorder, Heutink, Greenfield, and Robertson (1999) have also shown improvements of tactile detection by vision in a right-brain-damaged patient. That is, this patient performed significantly better when non-informative visual stimuli (i.e, lights) were presented together with tactile stimuli next to a rubber hand (which had the same orientation as the patients' own covered hand) compared to when visual stimuli were presented in the same location but next to the experimenter's hand. As rubber hands are often experienced as one' own hands (see Pavani et al., 2000), these authors suggest that non-informative vision of one's 'own' body parts, compared to someone else's, may modulate the effect of visual stimuli on tactile perception in that right-brain-damaged patient. Importantly, the patient in Rorder et al.'s study had very low false alarm rates for visual stimuli in a visual detection task in which no tactile stimuli were presented, and furthermore under this condition he reported to have felt touch in very few trials. Taken together, these results suggest that the presence of a visual stimulus next to a rubber hand (experienced as the patient's own hand) increases tactile sensitivity rather than response bias to touch.

Furthermore, another study (Làdavas et al., 2000) in right-brain-damaged patients has reported crossmodal visuo-tactile extinction (i.e., decrease in detection of contralesional tactile stimuli by the simultaneous presentation of visual stimuli near the ipsilesional hand) to occur specifically under conditions when the patients' hands were visible, with only mild crossmodal effects observed when their hands were occluded from view. Moreover, Serino and colleagues (Serino, Farnè, Rinaldesi, Haggard, & Làdavas, 2007) found that viewing the relevant body part, compared to a neutral object at the same location, enhanced tactile performance in a two point discrimination task in brain-damaged patients with somatosensory deficits, as well as in neurologically unimpaired participants. Notably, in the latter this facilitation was present in inverse relation to their tactile acuity, with greater improvements in individuals with lower tactile sensitivity. Such improvement in tactile spatial resolution did not occur when participants observed a rubber hand rather than their own hand, suggesting that this effect may not be explained by visual salience of the stimulated body part (Serino et al., 2007).

2.2 Interactions between vision of the body and attention: previous evidence and open questions

The neuropsychological findings described above are in line with what has been shown in healthy individuals: that viewing the body improves tactile perception. Furthermore, as some of the brain-damaged patients in the studies illustrated above exhibited attentional deficits, the pattern of results from these studies may also suggest an interplay between vision of the body and attentional factors in influencing tactile processing. However, from these findings it is not possible to draw any specific conclusions about how the interaction between these two factors may work.

While an ever-growing number of studies have been carried out on VET (as it has been shown by the concise review of the most relevant studies in this chapter), few investigations have looked at the role of visual information about the body on tactile spatial selection. One study using PET (Positron Emission Tomography) (Macaluso, Frith, & Driver, 2000b) has reported a different pattern of tactile-spatial attention modulations (i.e., greater activations for tactile stimuli presented at the currently attended, compared to the unattended, hand) under conditions when participants performed a tactile attention task with their eyes open compared to closed. That is, while in the postcentral gyrus (i.e., primary somatosensory area, SI) spatial attention effects were present irrespective of whether participants had their eyes open or closed during the task, in the intraparietal sulcus, a multimodal region involved in spatial representation and attention, these attentional modulations were only observed under conditions when participants had their eyes open. Although these findings suggest that attention and vision may interact in modulating tactile processing, from this study it cannot be resolved whether vision of the body or ambient visual-spatial information (or perhaps both) is the crucial factor that influences attentional effects in touch. Indeed, vision of the environment provides a frame of reference to localize events in external coordinates also in modalities other than vision (Röder, Rösler, & Spence, 2004; Warren, 1970), and therefore it could be expected to help attentional selection compared to when only proprioception information is available (i.e., when participants have their eyes closed, or are blindfolded). On the other hand, previous studies have shown that vision of the body, rather than vision of the environment alone, is crucial for proprioceptive localization (van Beers, Sittig, & Denier van der Gon, 1996, 1999);

which may suggest that the sight of the body could be also important in spatial selection (i.e., tactile-spatial attention). This issue will be discussed further in Chapther 5.

In addition, from Macaluso et al.'s study it cannot be directly established at which stages of somatosensory processing visual information concerning the body and attentional factors may interact. A recent ERP study (Forster & Eimer, 2005) has addressed the issue of whether, and at which stages, somatosensory processing may be modulated by vision of the stimulated body part and by gaze direction. Orienting one's gaze towards a body site improves tactile perception possibly by reinforcing the effects of spatial attention (see Honore' et al., 1988), which has been consistently shown to facilitate somatosensory processing (Eimer & Forster, 2003a, 2003b; Michie, Bearpark, Crawford, & Glue, 1987; Schubert, Ritter, Wüstenberg, Preuschhof, Curio et al., 2008). Accordingly, in the study by Forster and Eimer (2005), an enhancement of somatosensory ERPs was found for tactile stimuli presented to the hand towards which participants' gaze was directed compared to stimuli delivered to the other hand. In particular, under conditions when visual information concerning the stimulated body part was not available, this enhancement was present from about 140 ms after onset of tactile stimuli (i.e., overlapping with the somatosensory N140 component, which is thought to originate in secondary somatosensory cortex, SII; Frot & Mauguière, 1999), followed by a sustained negativity. By contrast, when participants were allowed to see the hand towards which their gaze was directed, earlier somatosensory components (i.e., P45 and N80, originating in primary somatosensory cortex, SI; Frot & Mauguière, 1999; Hari et al., 1984) were modulated, with greater amplitudes for tactile stimuli delivered at the hand participants' gaze was directed to. The findings from this study (Forster & Eimer, 2005) may suggest that vision of a body part facilitates effects of gaze orienting (and attention), although the experimental conditions with vision and no vision of the hand towards which the gaze was oriented to were not directly compared.

2.3 Summary and questions addressed in the studies presented in this thesis

The neural and behavioural evidence outlined in this chapter shows that providing visual information about the body parts touched modulates processing of tactile stimuli in both neurologically unimpaired people and in brain-damaged patients with somatosensory and/or attentional deficits. These visual modulations of touch may occur via feedback projections from multisensory brain areas involved in body representation

to early somatosensory areas, in particular the primary somatosensory cortex (SI), similarly to previous accounts of other crossmodal effects between vision and touch (see Macaluso, 2006 for a review). As described in Chapter 1, unimodal signals (e.g., visual and tactile) are believed to converge initially at subcortical level, in the superior colliculus, and subsequently in multisensory brain areas in frontal and parietal cortices, which contain bimodal neurons with overlapping visual and tactile receptive fields. Recurrent feedforward and feedback projections from these multimodal regions would then modulate activity in somatosensory areas that have been considered unimodal, such as SI.

As suggested at the beginning of this chapter, crossmodal interactions between touch and vision of the body, however, somewhat differ from classic multisensory effects whereby abrupt events in one modality (e.g., light flashes) interact with stimuli in a different sensory modality (e.g., touch). Indeed, the body itself is not only a (continuous) visual stimulus, but it is the recipient of tactile stimulation and the spatial frame within which tactile events are experienced. Furthermore, visual input about the body enhances the representation of the body space by providing spatial information about the body itself and the space around it. This may specifically suggest an interplay between vision of the body and spatial attention and selection in touch. Yet, this latter issue has hitherto received little attention in the literature. As illustrated above, from the study by Macaluso et al. (2000b) it cannot be concluded whether (continuous) vision of the body parts (i.e., the hands), rather than ambient visual-spatial information in general, is crucial in accounting for the visual modulations of attentional effects in touch obtained when participants had their eyes open, compared to closed, while performing a tactile-selection task.

The study presented in Chapter 5 of this thesis has investigated the role of visual input (ambient visual-spatial information and vision of the relevant body parts) in modulating tactile-spatial selection, using electrophysiological (ERP) and behavioural measures. This study has aimed to clarify the neural mechanisms underlying visual modulations of sustained tactile-spatial attention, and to investigate at which stages of somatosensory processing these effects may take place. The study presented in Chapter 6 has been carried out in right-brain-damaged patients with spatial attention impairments. In the neuropsychological literature, a number of previous studies have shown that in right-brain-damaged patients with tactile neglect and extinction viewing the relevant body parts improves perception of contralesional tactile stimuli (see above,

Halligan et al., 1996; Làdavas et al., 2000; Serino et al., 2007). Furthermore, contralesional tactile perception has been also shown to be enhanced following changes in hand posture (such as crossing the hands over the body midline) that result in the patients' left contralesional hand being placed in the ipsilesional 'non-neglected' hemispace. In the study presented in Chapter 6, we have specifically investigated whether viewing the stimulated body part (i.e., left contralesional hand) modulates the effects of this posture change (namely, crossing of the left hand) in right-brain-damaged patients.

Chapter 3

An ERP investigation on visuo-tactile interactions in peripersonal and extra-personal space: evidence for the spatial rule

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The spatial rule of multisensory integration holds that crossmodal stimuli presented from the same spatial location result in enhanced multisensory integration. The present study investigated whether processing within somatosensory cortex reflects the strength of crossmodal visuo-tactile interactions depending on the spatial relationship between visual and tactile stimuli. Visual stimuli were task-irrelevant, and were presented simultaneously with touch in peripersonal and extrapersonal space, in the same (congruent) or opposite (incongruent) hemispace with respect to the tactile stimuli. Participants directed their attention to one of their hands to detect infrequent tactile target stimuli at that hand while ignoring tactile targets at the unattended hand, all tactile non-target stimuli, and any visual stimuli. Enhancement of ERPs recorded over and close to somatosensory cortex was present as early as 100 ms after onset of stimuli (i.e., overlapping with the P100 component) when visual stimuli were presented next to the site of tactile stimulation (i.e., peri-hand space) compared to when these were presented at different locations in peripersonal or extra-personal space. Therefore, this study provides electrophysiological support for the spatial rule of visual-tactile interaction in human participants. Importantly, these early crossmodal spatial effects occurred regardless of the locus of attention. In addition, and in line with previous research, we found attentional modulations of somatosensory processing to be only present in the time range of the N140 component and for longer-latencies with an enhanced negativity for tactile stimuli at attended compared to unattended locations. Taken together, the pattern of the results from this study suggests that visuo-tactile spatial effects on somatosensory processing occur prior and independent of tactile-spatial attention.

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3.1 Introduction

Research in the last two decades has provided evidence that spatial representations of tactile and visual events occurring in the space immediately surrounding the body (i.e., peripersonal space; see Rizzolatti et al., 1997) are coded by an integrated visuo-tactile system centred on body parts (i.e., hand-centred) (Bremmer et al., 2001a; Duhamel et al., 1991, 1998; Fogassi et al., 1996; Graziano & Gross, 1993, 1995; Graziano et al., 1997; Rizzolatti et al., 1981). Single-cell recordings from several brain structures of the macaque monkey, such as the putamen and some parietal and premotor cortical areas, have revealed the existence of bimodal neurons that respond to both somatosensory and visual inputs. The visual receptive fields of these neurons are located on body parts (e.g., the hand), extending a few centimetres into the surrounding area and are in spatial register with the location of the neurons' tactile receptive fields. Furthermore, the rate of discharge of these neurons has been found to decrease as the distance between visual stimuli and the body part touched increases, according to the spatial rule of multisensory integration (see Stein & Meredith, 1993; Stein & Stanford, 2008).

It has been suggested that a neural system representing visuo-tactile peripersonal space, and peri-hand space in particular, operates in humans with similar properties to those shown in macaque, such as the constraint of spatial proximity between visual and tactile signals (Bremmer et al., 2001b; Làdavas, 2002; Làdavas et al., 1998; Macaluso, 2006; Macaluso & Driver, 2005). Studies on brain-damaged people have shown modulatory effects of visual stimuli on tactile perception that are dependent on spatial proximity between visual and tactile inputs (see Làdavas et al., 1998, 2000). These studies have reported that tactile extinction, that is, the decrease of contralesional tactile detection by the simultaneous presentation of an ipsilesional touch (Heilman et al., 1993; Moscovitch & Behrmann, 1994), can be significantly reduced if a task-irrelevant visual stimulus is presented concurrently next to the contralesional hand (i.e., peri-hand space) (di Pellegrino, Làdavas, & Farnè, 1997; Làdavas et al., 1998). In contrast, if visual stimuli are presented in a region of space beyond the space immediately surrounding the stimulated body parts (i.e., ~35 cm), tactile extinction is only weakly reduced (Làdavas et al., 1998). These findings are in support of the spatial rule of multisensory integration; although, a possible caveat is that because the location of task-irrelevant visual stimuli in radial space (near vs. far) was manipulated in separate blocks

of trials, it cannot be ruled out that a different distribution of spatial attention in 'near-' and 'far-space' blocks may also account for the effects on tactile processing (see Chapter 1 section 1.8, and section 3.5 of this chapter for further discussion of this issue).

The neural basis of visuo-tactile interactions in humans has been studied in recent years using both heaemodynamic and electrophysiological measures. For instance, recent fMRI (functional magnetic resonance imaging) studies have shown that activity in heteromodal (e.g., intraparietal sulcus; IPS) as well as in modality-specific (i.e., occipital and somatosensory) brain areas is enhanced for spatially congruent compared to incongruent visuo-tactile bimodal stimulation (Macaluso, et al., 2002b, 2005). In these studies visual stimuli were always presented in peripersonal space, either close to the site of tactile stimulation (i.e., hand) or at a distance from it. However, unlike neuropsychological studies, fMRI studies have not compared brain responses to visuo-tactile bimodal stimulation under near and far space conditions.

To date two ERP studies have investigated spatial constraints of visuo-tactile interactions in the human brain using simultaneous presentation of visual and tactile stimuli (Piesco et al., 2005; Schürmann et al., 2002). In these studies, ERPs obtained in response to simultaneous bimodal stimulation were compared with the algebraic sum of ERP responses to unimodal single stimuli (see Gondan & Röder, 2006; Macaluso & Driver, 2005; Stanford & Stein, 2007 for a critical discussion of this method). In one of these studies (Piesco et al., 2005) bimodal interaction effects (i.e., differences between ERP responses to bimodal stimulation compared to the sum of unimodal responses) were found to be present regardless of whether visual and tactile stimuli were presented at the same or different locations in peripersonal space. In the other study (Schürmann et al., 2002), visual stimuli were presented in far extra-personal space either in the same or the opposite hemispace to tactile stimuli. In this study bimodal interaction effects were found to occur regardless of the location of the visual stimuli at some electrode sites; while at other sites only bimodal stimuli presented in the same hemispace showed a different pattern of ERP responses compared to the sum of the single inputs. From these studies it is not clear whether and to what extend spatial congruence plays a role in visuo-tactile interactions. However, it has been argued that spatial effects in multisensory paradigms are less likely to be present in low complexity tasks (Forster et al., 2002; Gondan et al., 2005; Posner, 1978). Likewise, in the previous ERP studies participants were either performing a simple detection task (Piesco et al., 2005) or were not engaged in any task (Schürmann et al., 2002).

The aim of the present study was to investigate whether ERPs elicited by tactile stimuli coupled with task-irrelevant visual stimuli are modulated by the spatial relationship between tactile and visual stimuli in accordance with the spatial rule of multisensory integration; the rationale being that ERP responses should reflect the extent of visual-tactile interactions under different spatial configurations. In particular, and differently from previous studies on multisensory integration that focussed on non-linear-responses (e.g., Piesco et al., 2005; Schürmann et al., 2002), the present study looked specifically at whether the location of task-irrelevant visual stimuli modulates behavioural and electrophysiological responses associated with processing within somatosensory cortex (i.e., ERPs recorded over and close to somatosensory cortex). To this aim the visual stimuli were always presented concurrently with tactile stimuli in peripersonal ('near-space') or far extra-personal space ('far-space'), either in the same (congruent) or opposite (incongruent) hemispace as tactile stimuli. Participants were required to direct their attention to one hand in order to detect tactile target stimuli delivered on that hand. According to previous studies (Duhamel et al., 1991; Graziano & Gross, 1993; Làdavas et al., 1998; Macaluso et al., 2005), we expected ERPs to be modulated by the distance of visual stimuli from the site of tactile stimulation, with enhancement of ERPs under conditions in which visual stimuli were presented at the same location as tactile stimuli compared to conditions in which the former were presented at a different location in peripersonal or extra-personal space. In addition, we expected tactile-spatial attention to modulate somatosensory processing with enhanced ERPs in response to tactile stimuli delivered to the currently attended, compared to unattended, hand (e.g., Desmedt & Robertson, 1977; Eimer & Forster, 2003a, 2003b; Michie, 1984; Michie et al., 1987).

3.2 Materials and Methods

3.2.1 Participants

15 paid volunteers took part in the experiment. Three had to be excluded due to an excess of alpha waves. Thus, 12 participants (3 males and 9 females), aged between 23 and 36 years (average age: 26.8 years) remained in the sample. All participants were right-handed; and all had normal or corrected-to-normal vision by self-report. The experiment was approved by the Ethics Committee, City University, London; and all participants gave their written informed consent.

3.2.2 Stimuli and Apparatus

Participants sat in a dimly lit sound-attenuated experimental chamber resting their arms on a table in front of them. Two sets of two small boxes (3 x 5 x 3 cm) were each placed equidistant to the left and right of the participants' midline at a distance of 40 cm and 110 cm from the participants' body respectively (see Fig. 3.1). Each box had one tactile stimulator and one red LED (light-emitting diode) embedded in its surface, the LED being 1.5 cm distant from the tactile stimulator. Participants' index fingers were placed on top of the set of boxes closest to them, covering the tactile stimulators. The distance between participants' index fingers was 40 cm.

On each trial one tactile and one visual stimulus were presented simultaneously. Tactile stimulation was provided using 12V solenoids driving a metal rod with a blunt conical tip to the top segment of the index finger making contact with the fingers whenever a current was passed through the solenoid. Tactile non-target stimuli consisted of one rod tip contacting participants' index finger for 200 ms. Tactile target stimuli were infrequent and had a gap of 4 ms in the continuous contact after a duration of 98 ms. Task-irrelevant visual stimuli were provided by 5 mm LEDs that were illuminated for 200 ms.

Each participant completed two experimental conditions: 'near-space' and 'far-space'. The two experimental conditions differed in the locations of visual stimuli; in the 'near-space' condition the visual stimuli were always presented close to the participants' hands, that is, on the set of boxes where the fingers were placed; in the 'far-space' condition the visual stimuli were always presented on the set of boxes that were located at a distance of 70 cm from the participants' hands (see Fig. 3.1).

Participants were instructed to keep their gaze on a small white fixation square (0.64 cm^2) placed half-way between the two set of boxes at a distance of 75 cm from the participants' body. White noise (50 dB, measured from the position of the participant's head) was presented from two loudspeakers placed at 110 cm from the participants' head and equidistant to the right and left of the midline, to mask any sounds made by the tactile stimulators.

Participants responded by pressing a button with either foot. Half of participants used their left foot and the other half used their right foot to respond to targets. The foot they had to use to give their responses was assigned at the beginning of the experimental session and was kept constant throughout the two experimental conditions.

Experimental setup

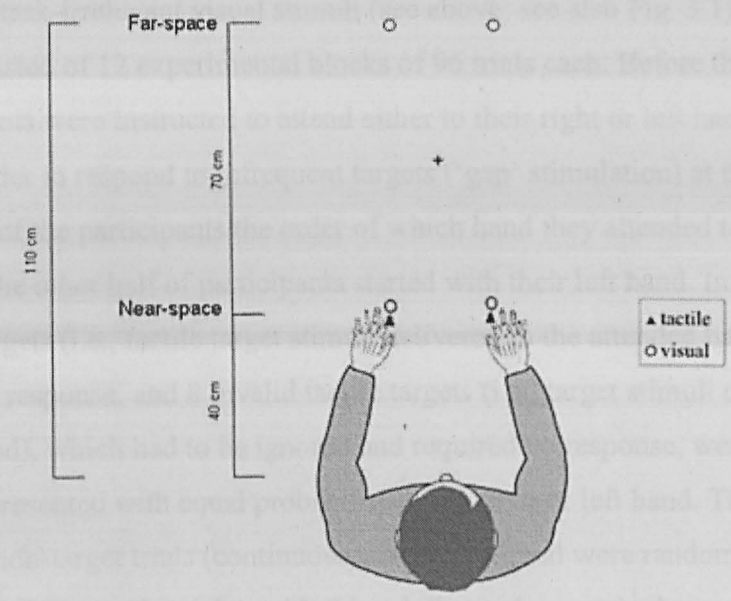


Figure 3.1 Schematic representation of the experimental setup showing the sites of tactile stimulation and the four possible locations of visual stimuli in 'near-space' and 'far-space', and in the two hemispaces. On the left side, the actual distance of the visual stimuli from the participants' body is given.

3.2.3. Procedure

At the start of the experimental session participants carried out two pre-experimental blocks of 48 trials each to ensure they could detect the visual stimuli and discriminate the tactile stimuli that they would receive during the experiment. In the first block only visual stimuli were presented and participants had to respond to all of them. The visual stimuli were presented randomly and with equal probability at one of the four possible locations (Fig. 3.1). In the second block only tactile stimuli were delivered and participants had to respond to all tactile target stimuli ('gap' stimulation) while ignoring tactile non-target stimuli (continuous stimulation). Tactile targets were delivered randomly on half of the trials (i.e., 24 trials) with equal probability to the right and the left hand. Participants started the experimental session only when their accuracy in the two pre-tests was 75% or above. The data of the pre-experimental blocks was not analyzed further. Following the pre-test, each participant completed the two

experimental conditions: 'near-space' and 'far-space'. Half of the participants performed the 'near-space' condition first followed by the 'far-space' condition; for the other half this order was reversed. The two experimental conditions differed only in the location of the task-irrelevant visual stimuli (see above; see also Fig. 3.1). Each condition consisted of 12 experimental blocks of 96 trials each. Before the start of each block participants were instructed to attend either to their right or left hand throughout the block in order to respond to infrequent targets ('gap' stimulation) at the attended hand. For half of the participants the order of which hand they attended to was right-left-right-etc; the other half of participants started with their left hand. In each block 8 valid tactile targets (i.e., tactile target stimuli delivered to the attended hand) which required a foot response, and 8 invalid tactile targets (i.e., target stimuli on the unattended hand), which had to be ignored and required no response, were delivered. Targets were presented with equal probability to the right or left hand. The remaining 80 trials were non-target trials (continuous stimulation) and were randomly presented with equal probability to the right and left hand; these also required no response. Visual stimuli were always presented simultaneously with tactile stimuli, with equal probability either in the same or opposite hemispace with respect to the tactile stimulus. Participants were instructed to ignore all visual stimuli throughout the experiment. Visual and tactile stimuli were delivered after 300 ms from the beginning of each trial. From the stimulus onset, participants had 1200 ms to respond. The inter-trial interval (ITI) before the start of the next trial was randomly set between 200 and 600 ms. Participants were instructed to maintain fixation at the fixation point throughout each block and this was monitored throughout the experiment via a camera.

3.2.4. Recording and Data Analysis

EEG (electroencephalogram) was recorded with Ag-AgCl electrodes and linked-earlobe reference from 28 scalp electrodes (midline electrodes: Fz, Fcz, Cz, Pz; electrodes over the right hemisphere: Fp2, F4, F8, Fc2, Fc6, C4, T8, Cp2, Cp6, P4, P8, O2 and the homologous electrode sites over the left hemisphere), using BrainVision recording system (BrainAmp amplifier and BrainVision Recorder software, version 1.02; Brain Products GmBH, Gilching, Germany; http://www.brainproducts.com). The amplifier bandpass was 0.01-100 Hz. Horizontal electrooculogram (HEOG) was recorded bipolarly from the outer canthi of both eyes. Electrode impedance was kept below 5 kΩ. EEG and EOG were sampled with a 500 Hz digitization rate, and

subsequently were digitally filtered off-line with a 40 Hz low pass filter. EEG data were analyzed using BrainVision Analyzer software (version 1.05) (Brain Products GmBH, Gilching, Germany). EEG and EOG were epoched off-line into 700 ms periods, starting 100 ms before and ending 600 ms after the onset of tactile stimuli. ERPs for tactile non-target stimuli were averaged relative to a 100-ms pre-stimulus baseline. Trials with eyeblinks (Fp1 or Fp2 exceeding ± 60 μV relative to baseline), horizontal movements (HEOG exceeding ± 30 μV relative to baseline, approximately equal to ±2.5° of visual angle; see Mangun & Hillyard, 1991) (7% of the total trials on average) or other artifacts (a voltage exceeding ± 60 μV relative to baseline at electrodes Fc6, C4, Cp2, Cp6, P4, P8, O2 and at homologous electrode sites over the left hemisphere) measured within 600 ms after stimulus onset (22% of the total trials on average), were excluded from analysis. ERP analysis was restricted to only non-target trials in which participants responded correctly. Trials immediately following a response were excluded from analysis (10% of total trials on average) in order to avoid contamination of averaged ERPs by movement-related artifacts. The number of trials left for inclusion in each single-subject average ranged between 124 and 172 per each condition (i.e. 'near-space-congruent', 'near-space-incongruent', 'far-space-congruent', 'far space-incongruent'), including attended and unattended trials. As the main aim of this study was to investigate crossmodal spatial effects on processing within somatosensory cortex, statistical analyses (repeated measures ANOVAs) were conducted for recording sites over and close to somatosensory areas (Fc5, Fc6, C3, C4, Cp1, Cp2, Cp5, Cp6, P3, P4, P7 and P8), where somatosensory ERP components are largest[4]. ERP mean amplitudes were computed within successive measurement windows centred on the latencies of early somatosensory ERP components: P100 (80-125 ms after stimuli onset) and N140 (125-175 ms after stimuli onset). Mean amplitudes were also computed for the time interval of 180 and 295 ms post-stimuli in order to investigate longer-latency effects. The choice of the time epochs included in the analysis was based on earlier reports on crossmodal *spatial* effects, and on visual inspection of the grand averages.

To investigate crossmodal effects and effects of tactile-spatial attention on ERPs overall statistical analysis (repeated measures ANOVA) included the factors space

[4] Throughout this chapter we refer to ERPs measured *over and close to somatosensory cortex*. As expected, ERP waveforms at the recording sites included in the statistical analysis show the typical pattern of somatosensory ERP components (P45, N80, P100, and N140) in response to tactile stimuli. Although, as task-irrelevant visual stimuli were always presented concurrently with tactile stimuli, contributions from visual ERP responses as well as multisensory superadditive and subadditive effects may also be present in the ERP waveforms.

(near-space vs. far-space), congruence (congruent vs. incongruent), attention (attended vs. unattended), electrode site (see above), and hemisphere (contralateral vs. ipsilateral to the stimulated hand). To investigate crossmodal effects on response speed to tactile stimuli, repeated measures ANOVA was performed on mean reaction times (RTs) to tactile target stimuli delivered at the attended hand, with the factors space (near-space vs. far-space), congruence (congruent vs. incongruent), and hand (left vs. right hand).

3.3 Results

3.3.1 Behavioural data

The participants' task was to direct their attention to one hand to detect infrequent tactile target stimuli on that hand while ignoring tactile target stimuli at the other hand and any tactile non-target stimuli. On each trial task-irrelevant visual stimuli were presented either in near or far space in the same or opposite hemispace as tactile stimuli (i.e., 'near-space-congruent', 'near-space-incongruent', 'far-space- congruent', and 'far-space-incongruent' trials). There was no significant difference between the number of missed tactile targets between the conditions 'near-space-congruent', 'near-space-incongruent', 'far-space- congruent', and 'far-space-incongruent' (Table 3.1), and the overall rate of false alarms to non-target stimuli was below 1%. All trials in which a correct response was given were entered in the analysis. RTs in individual trials never exceeded the participant's average +3 SD (standard deviations). Participants were faster at responding to tactile targets when task-irrelevant visual stimuli were presented at the same location as tactile stimuli (494.3 ms; 'near-space-congruent' trials) than when these were presented at a distance from the stimulated hand either in peripersonal (510.6 ms; 'near-space-incongruent' trials) or in far extrapersonal space (520.2 and 513.4 ms; 'far-space- congruent'and '-incongruent' trials, respectively) (Table 3.1). Overall analysis comparing mean RTs to tactile targets on 'near-space-congruent' and '-incongruent' and 'far space-congruent' and '-incongruent' trials showed a space x congruence interaction ($F_{[1,11]} = 6.12$, $p < 0.02$). Pairwise comparisons showed that participants responded significantly faster to tactile targets delivered on 'near-space-congruent' trials compared to 'near-space- incongruent' trials ($F_{[1,11]} = 8.31$, $p < 0.02$), and compared to trials in which visual stimuli were presented at a distance from the hands in far extrapersonal space ('far-space-congruent' and '-incongruent' trials; $F_{[1,11]} = 9.18$, $p < 0.01$ and $F_{[1,11]} = 8.27$, $p < 0.02$, respectively). The comparison between

'far-space-congruent' and '-incongruent' trials was not significant ($F_{[1, 11]} = 2.67$, $p = 0.21$). In addition, mean RTs to tactile targets delivered on 'near-space-incongruent' trials did not differ significantly from 'far-space- congruent' and '-incongruent' trials ($F_{[1, 11]} = 3.87$ $p = 0.18$, and $F_{[1, 11]} = 0.64$, $p = 0.65$, respectively).

Behavioural results (accuracy and mean RTs)

	Near-space		Far-space	
	Congruent	**Incongruent**	**Congruent**	**Incongruent**
Missed responses	2.3%	3.8%	2.7%	3.1%
Mean RTs	494.3 ms	510.6 ms	520.2 ms	513.4 ms

Table 3.1 Percentage of missed responses and mean RTs to tactile target stimuli under conditions when task-irrelevant visual stimuli were presented in 'near-space' and in 'far-space', in the same (congruent) and opposite (incongruent) hemispace as touch. Mean RTs reported in the table are collapsed across the left and right hands.

3.3.2 ERP Results

Crossmodal spatial effects and effects of tactile-spatial attention on ERPs recorded over and close to somatosensory cortex were determined by comparing ERPs obtained for tactile non-target stimuli at the attended and unattended hand when task-irrelevant visual stimuli were presented in near and far space in the same (congruent) or opposite (incongruent) hemispace as tactile stimuli (i.e., 'near-space-congruent', 'near-space-incongruent', 'far-space-congruent', and 'far-space-incongruent' trials).

Figure 3.2 and 3.3 show crossmodal spatial effects and tactile-spatial attention effects on ERPs at electrode sites over and near the somatosensory cortex, in the 'near-space' and 'far-space' conditions, respectively. In each figure, grand-averaged ERPs are shown separately for 'congruent' (*solid lines*), and 'incongruent' (*dashed lines*) trials for stimuli presented at tactually attended (in *black*) and unattended (in *grey*) locations, at electrodes contralateral and ipsilateral (left and right half of the figure, respectively) to the site of tactile stimulation. Figure 3.4 shows overall crossmodal spatial modulations on ERPs in the 'near-space' (in *black*) and 'far-space' (in *grey*) conditions collapsed across 'attended' and 'unattended' trials, at one of the electrodes (i.e., C3/4c; over somatosensory cortex, contralateral to the site of tactile stimulation).

For the time range of the P100 component, ERPs for tactile stimuli coupled with spatially coincident visual stimuli ('near-space-congruent' trials) appear to be enhanced

in comparison to ERPs elicited on 'near-space-incongruent' trials; however this difference appears to be only present at electrode sites contralateral to the site of tactile stimulation. ERPs in 'far-space' trials do not appear to be modulated by the relative location of visual stimuli (i.e., in the congruent or incongruent hemispace to touch). In addition, as can be see in Figure 3.4, ERPs elicited in the 'near-space-congruent' trials are enhanced compared to ERPs obtained on 'far-space' trials (for both '-congruent' and '-incongruent' trials) in the P100 time range.

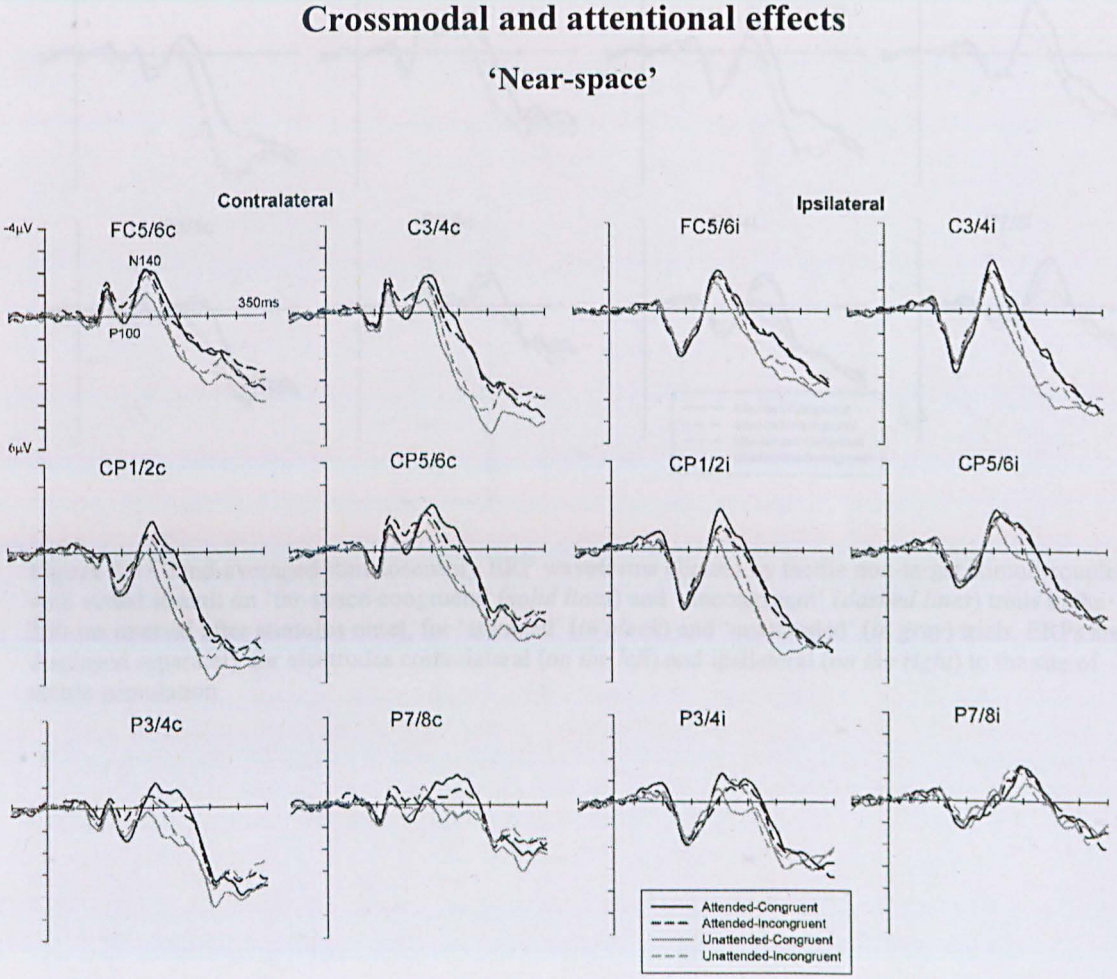


Figure 3.2 Grand-averaged somatosensory ERP waveforms elicited by tactile non-target stimuli presented with visual stimuli on 'near-space-congruent' (*solid lines*) and '-incongruent' (*dashed lines*) trials in the 350-ms interval after stimulus onset, for 'attended' (*in black*) and 'unattended' (*in grey*) trials. ERPs are displayed separately for electrodes contralateral (*on the left*) and ipsilateral (*on the right*) to the site of tactile stimulation.

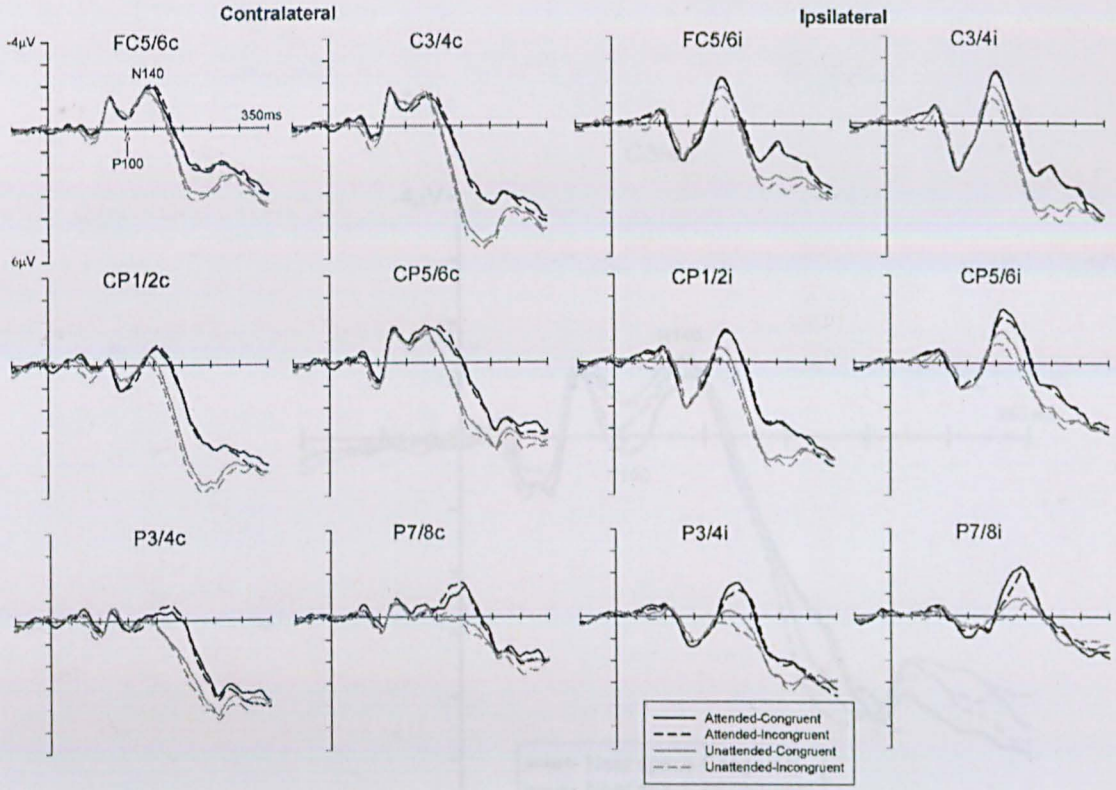


Figure 3.3 Grand-averaged somatosensory ERP waveforms elicited by tactile non-target stimuli coupled with visual stimuli on 'far-space-congruent' (*solid lines*) and '-incongruent' (*dashed lines*) trials in the 350-ms interval after stimulus onset, for 'attended' (*in black*) and 'unattended' (*in grey*) trials. ERPs are displayed separately for electrodes contralateral (*on the left*) and ipsilateral (*on the right*) to the site of tactile stimulation

Crossmodal spatial-congruence effects

'Near-space' and 'Far-space'

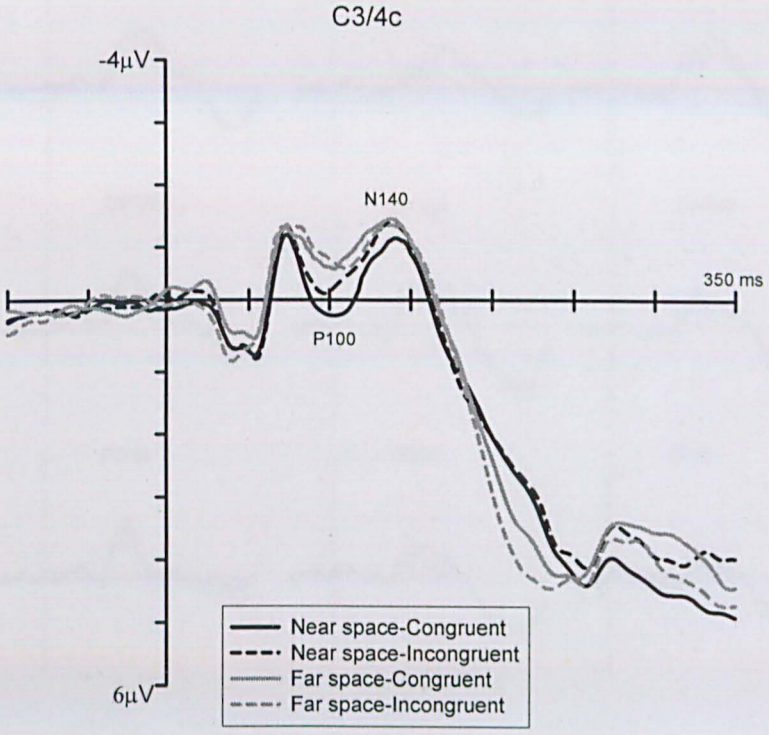


Figure 3.4 Grand-averaged ERPs elicited by tactile non-target stimuli coupled with spatially congruent (*solid lines*) vs. incongruent (*dashed lines*) visual stimuli in the 'near-space' (*in black*) and 'far-space' (*in grey*) conditions, at one of the electrode sites included in the analysis (i.e., C3/4c; over somatosensory cortex, contralateral to the site of tactile stimulation). Crossmodal spatial effects (i.e., enhancement of ERPs for spatially congruent vs. incongruent visual-tactile stimuli) can be observed in the 'near-space' but not in the 'far-space' conditions (see the Results section for details).

Figure 3.5 shows attentional modulations of ERPs recorded over and near somatosensory cortex. The figure displays difference ERP waveforms obtained by subtracting ERPs elicited in 'unattended' trials from ERPs in 'attended' trials, separately for the 'near-space' (*solid lines*) and the 'far-space' (*dashed lines*) conditions. As can be seen from the figure, attentional modulations do no appear to differ substantially between the two conditions.

Attentional effects

Difference waveforms: 'Near-space' and 'Far-space'

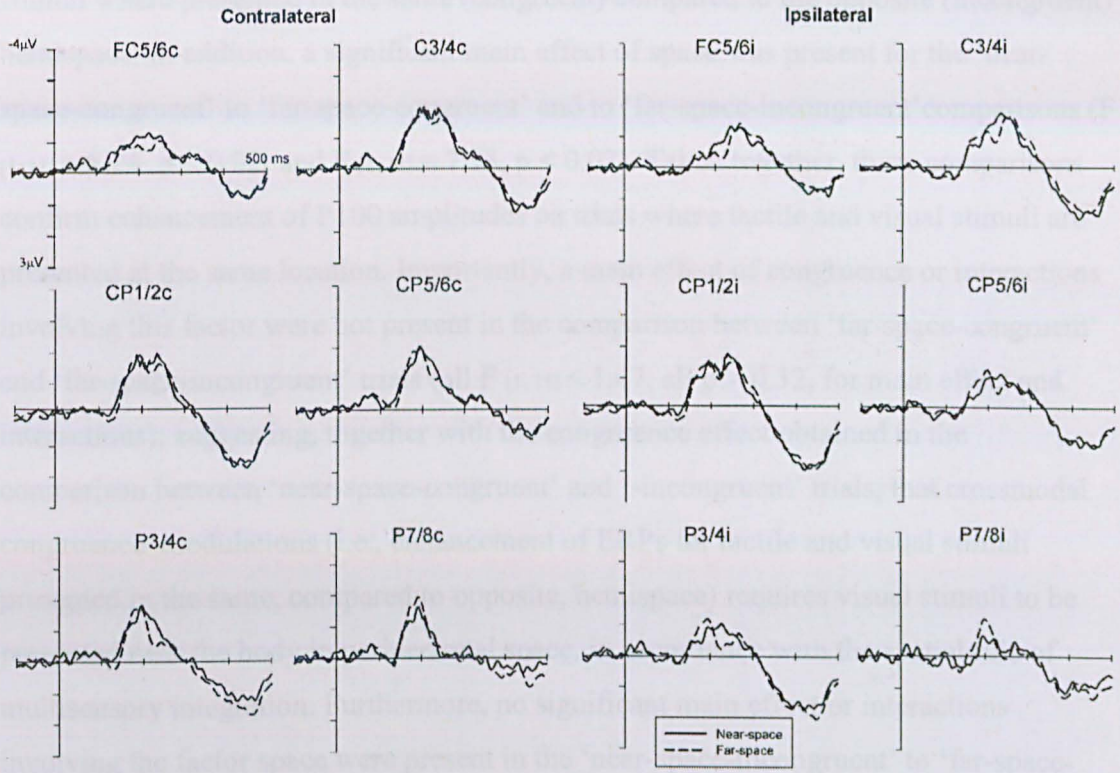


Figure 3.5 Difference ERP waveforms obtained subtracting ERPs in response to non-target stimuli in 'unattended' trials from ERPs in the 'attended' trials in the 500-ms time interval following stimuli onset, separately for the 'near-space' (*solid lines*) and the 'far-space' (*dashed lines*) conditions.

Statistical analyses confirmed these observations[5]. In the overall analysis comparing ERPs to tactile stimuli under attended and unattended conditions for the factors space and congruence (see above), a significant main effect of space was present in the P100 time range (80-125 ms post-stimuli onset) ($F_{[1, 11]} = 6.061$, $p < 0.04$), indicating overall enhancement of ERPs for 'near-space' compared to 'far-space' trials in this time range. A space x congruence x hemisphere interaction was also present in this time interval ($F_{[1, 11]} = 5.94$, $p < 0.04$). Follow-up comparisons (ANOVAs) were carried out between ERPs for all combinations of trial types (see above). For the 'near-space-congruent' to 'near-space-incongruent' comparison a congruence x hemisphere interaction ($F_{[1, 11]} = 13.97$, $p < 0.004$) was present and follow-up analyses separate for electrodes over the two hemispheres showed a significant main effect of hemispace only

[5] Only two- and three-way interactions are reported.

at electrodes contralateral to the site of tactile stimulation ($F_{[1, 11]} = 8.23$, $p < 0.02$), indicating that when visual stimuli were presented in near space ERPs recorded from the hemisphere contralateral to touch were enhanced for trials where visual and tactile stimuli where presented in the same (congruent) compared to the opposite (incongruent) hemispace. In addition, a significant main effect of space was present for the 'near-space-congruent' to 'far-space-congruent' and to 'far-space-incongruent'comparisons ($F_{[1, 11]} = 8.24$, $p < 0.02$; and $F_{[1, 11]} = 7.93$, $p < 0.02$). Taken together, these comparisons confirm enhancement of P100 amplitudes on trials where tactile and visual stimuli are presented at the same location. Importantly, a main effect of congruence or interactions involving this factor were not present in the comparison between 'far-space-congruent' and 'far-space-incongruent' trials (all $F_{[1, 11]} < 1.47$, all $p > 0.32$, for main effect and interactions); suggesting, together with the congruence effect obtained in the comparison between 'near-space-congruent' and '-incongruent' trials, that crossmodal congruence modulations (i.e., enhancement of ERPs for tactile and visual stimuli presented in the same, compared to opposite, hemispace) requires visual stimuli to be presented near the body in peripersonal space, in accordance with the spatial rule of multisensory integration. Furthermore, no significant main effect or interactions involving the factor space were present in the 'near-space-incongruent' to 'far-space-congruent' and to 'far-space-incongruent' comparisons. These latter comparisons indicate that ERPs obtained under conditions when visual stimuli are presented at a different location as tactile stimuli either in near or far space are statistically the same. Importantly, no interactions between the factor attention and space and/or congruence were obtained in any of the above analyses for the P100 range, and further, additional follow-up analysis comparing ERPs only on 'near-space-congruent' trials under attended and unattended conditions in this time range revealed no significant main effect or interactions involving the factor attention, suggesting that crossmodal interaction effects on 'near-space-congruent' trials occurred regardless of whether or not attention was directed to the site of tactile stimulation. A significant main effect of hemisphere was also present in the P100 time range ($F_{[1, 11]} = 40.61$, $p < 0.001$), with overall enhanced amplitudes over the hemisphere ipsilateral compared to contralateral to the site of tactile stimulation.

For the subsequent analysis window of the N140 component (125-175 ms post-stimuli) initial overall analysis showed a significant main effect of attention ($F_{[1, 11]} = 9.47$, $p < 0.02$) and an attention x hemisphere interaction ($F_{[1, 11]} = 18.30$, $p < 0.001$),

confirming the presence of larger N140 amplitudes for tactile stimuli at the currently attended compared to the unattended hand (see Fig. 3.5). In addition, a space x congruence x attention interaction ($F_{[1,11]} = 8.56$, $p < 0.02$) was obtained and follow-up analyses revealed that the main effect of attention reached statistical significance on 'near-space-congruent' and 'far-space-congruent' and 'far-space-incongruent' trials (for all three comparisons $F_{[1,11]} > 7.31$, $p < 0.03$) but not on 'near-space-incongruent' trials ($F < 1$, $p = 0.43$)[6].

For later latencies (180-295 ms post-stimulus) a significant main effect of attention ($F_{[1,11]} = 28.83$, $p < 0.0001$) was present, reflecting an enhanced negativity for tactile stimuli at attended versus unattended locations (Fig. 3.3). In addition, a significant main effect of hemisphere was present ($F_{[1,11]} = 25.25$, $p < 0.0001$), indicating that in this time interval ERP amplitudes were more pronounced over the hemisphere contralateral to the site of tactile stimulation. No other main effects or interactions involving the factors attention, space and/or congruence were present indicating that attentional modulations of ERPs occurred irrespective of the spatial location of task-irrelevant visual stimuli[7].

[6] In order to investigate whether the space x congruence x attention interaction in the time range of the N140 component might indicate attentional modulations of crossmodal effects, two separate ANOVAs were carried out, one for the 'attended' and one for the 'unattended' trials. A space x congruence interaction was found for the 'unattended' trials ($F = 19.47$; $p < 0.0001$), and follow-up comparisons (ANOVAs) revealed a significant main effect of congruence in the comparison between 'near-space-congruent' and 'near-space-incongruent' trials ($F = 8.98$, $p < 0.03$), reflecting enhanced amplitudes for the latter ('-incongruent' trials). This difference may be explained by the lack of significant attentional modulations in the 'near-space-incongruent' trials (see Fig. 3.2 and Results section), resulting in enhanced ERPs elicited by unattended 'near-space-incongruent' trials compared to the unattended 'near-space-congruent' trials (see also the Discussion section for a detailed discussion of this latter finding). The other comparisons did not reveal any main effects or interactions involving the factors space and congruence (all $F < 1.45$, all $p > 0.28$). The interaction between space and congruence for the 'attended' trials was not significant ($F < 1$, $p = 0.74$). Taken together, these comparisons are not in support of a modulation of crossmodal effects by attention in this time range.

[7] We further tested whether tactile-spatial attention modulates ERPs recorded over visual cortex (i.e., at O1 and O2 electrodes) for the same time intervals as used in the other analyses. We compared ERPs obtained under conditions when visual stimuli were presented at tactually attended vs. unattended locations with the same factors used in the main analysis (see Methods). In the time interval between 125-175 ms post-stimuli, a main effect of attention approached significance ($F = 3.97$, $p = 0.075$), indicating that attending to tactile stimulus locations may result in weak attentional modulations over the visual cortex. Importantly, the interactions between attention and the factors space and congruence were not significant. No other main effects or interactions involving these factors were found in any of the other analysis time intervals.

3.4 Discussion

In the present study we investigated whether processing within somatosensory cortex reflects crossmodal interactions between tactile stimuli and task-irrelevant visual stimuli according to the spatial rule of visual-tactile integration, which predicts stronger crossmodal interactions between spatially coincident visual and tactile stimuli. Visual stimuli were presented simultaneously with touch close to the hands in peripersonal space ('near-space' condition) or 70 cm from the hands in far extra-personal space ('far-space' condition), and either in the same (congruent) or opposite (incongruent) hemispace with respect to the tactile stimuli. Participants had to direct their attention to one of their hands in order to detect infrequent 'gap' tactile target stimuli delivered to the attended hand while ignoring tactile targets at the unattended hand, all tactile non-target stimuli and any visual stimuli.

We found that response speed to tactile target stimuli was modulated by the relative spatial location of task-irrelevant visual stimuli. That is, participants' responses to tactile targets were faster when visual stimuli were presented at the same location as tactile stimuli compared to responses obtained under conditions when visual stimuli were presented at a different location in peripersonal and extra-personal space. Unlike RTs, response accuracies were not modulated by spatial congruence between visual and tactile stimuli, possibly due to the easiness of the task (ceiling effect). Importantly, the rate of false alarms (i.e., responses to any tactile non-target stimuli, and to tactile targets at unattended locations) was below 1% in every condition. This suggests that our results on RTs may not be explained by shifts in response criterion (i.e., occurring at a post-perceptual stage)[8], that is, to the participants being more willing to respond to tactile stimuli delivered at the location where visual stimuli are also presented. These data instead suggest an improvement at a perceptual level. To our knowledge, this is the first time that a near-far crossmodal (visuo-tactile) modulation has been shown in neurologically unimpaired people. This result is in agreement with previous studies in right-damaged patients that showed that task-irrelevant visual stimuli can enhance tactile perception when they are presented in the area surrounding the body part touched

[8]This result is also supported by the finding that crossmodal spatial-congruence modulates early ERP components, which are associated with perceptual stages of processing.

(i.e., peri-hand space), while these crossmodal effects are reduced or no longer present when visual stimuli are placed outside this area in far space (see Làdavas et al., 1998).

In line with the behavioural results, early ERPs recorded over and close to somatosensory cortex were found to be modulated by the spatial relationship between visual and tactile stimuli. In particular, the P100 component was enhanced for ERPs in response to tactile stimuli coupled with spatially congruent visual stimuli compared to ERPs obtained under conditions in which visual stimuli were presented at a distance from the site of tactile stimulation in near and far space. Under conditions when visual stimuli were presented in near space this enhancement was only present for ERP responses contralateral to the site of tactile stimulation, in agreement with previous imaging studies on multisensory interactions (Foxe et al., 2000; Macaluso et al., 2002b, 2005). Importantly, there was no statistical difference between trials in which visual stimuli were presented in far space in the same (congruent) and opposite (incongruent) hemispace to touch. This suggests, when considered together with the effect of spatial congruence in 'near-space' trials discussed above, that proximity of the visual stimuli to the body is required for the congruence modulations (i.e., differences in responses to visual-tactile stimuli presented in the same vs. opposite hemispaces) to be observed. In addition, and crucially, no reliable difference was present in the P100 time interval between conditions in which visual stimuli were presented at a distance from the site of tactile stimulation in peripersonal and far space; although on visual inspection of the graphs (Fig. 3.4), a gradient of crossmodal modulation can be observed between these conditions, with greater ERP amplitudes for the condition when visual stimuli were presented in near space. Taken together these results show that the spatial relationship between visual and tactile stimuli modulate early ERPs, with enhanced amplitudes for tactile stimuli coupled with visual stimuli delivered near the site of tactile stimulation (i.e., peri-hand space) compared to ERPs obtained when visual stimuli are presented at a different location in peripersonal or far space, as one would predict according to the spatial rule of multisensory integration (see Stein & Meredith, 1993; Stein & Stanford, 2008).

As noted above, these multisensory effects were present at relatively early stages of somatosensory processing. That is, an interaction between the factors space and hemispace was only observed in the P100 time interval and was not present at later stages of somatosensory processing. As the somatosensory P100 component is assumed to be generated in secondary somatosensory cortex (SII, i.e., a modality-specific area;

Frot & Mauguière, 1999; Hari et al., 1984), the crossmodal modulation of this component suggests that sensory-specific areas can be modulated by spatially congruent visual-tactile stimulation. This result is in line with recent fMRI studies that have shown that activity in modality-specific brain regions (i.e., the parietal operculum, corresponding to SII, as well as the occipital cortex) can be modulated by crossmodal interactions between visual and tactile stimuli at congruent locations (Macaluso et al., 2002b, 2005).

Our finding that the modality-specific P100 component was modulated by visuo-tactile interactions is compatible, in principle, with hierarchical models of multisensory integration that involve feedback projections from multimodal regions of convergence to unimodal somatosensory areas (Felleman & Van Essen, 1991; Jones & Powell, 1970), as well as with the proposal, based on recent neurophysiological evidence, that direct anatomical connections between sensory-specific brain areas are involved in multisensory integration (Cappe & Barone, 2005; Falchier et al., 2002; Ghazanfar & Schroeder, 2006; Schroeder & Foxe, 2005). Although these two models are not mutually exclusive, it has been suggested that unlike crossmodal modulations of very early ERPs (i.e., ~40-50 ms post-stimulus; see Giard & Peronnet, 1999 for auditory-visual; and Foxe et al., 2000; Murray et al., 2004 for auditory-tactile) that occur regardless of spatial congruence of bimodal stimuli and that may rely on direct influences between modality-specific areas, later crossmodal spatial effects on modality-specific ERPs (see Eimer, 2001; Eimer & Driver, 2000; Eimer et al., 2001) could be accounted for by top down modulations from heteromodal cortical regions (see also Macaluso & Driver, 2005). These spatially-specific crossmodal effects have been mostly reported for crossmodal spatial attention, and these have been shown to arise at around 100 ms after stimulus onset, similar to the effects found in this study.

Importantly, however, crossmodal spatial modulations of the somatosensory P100 in the current study were present regardless of whether or not attention was directed to the site of tactile stimulation. That is, the interactions of the factor attention with the factors space and congruence in the P100 range were not significant, and more specifically no significant difference was observed between ERPs in response to spatially coincident visual-tactile stimuli under attended and unattended conditions for the P100 time range. In contrast, attentional modulations were present at subsequent stages of processing; that is, attended tactile stimuli elicited an enhanced somatosensory N140 component followed by a sustained negativity compared to unattended tactile

inputs, in agreement with previous ERP studies on tactile-spatial attention (e.g., Desmedt & Robertson, 1977; Eimer & Forster, 2003a, 2003b; Garcia-Larrea, Lukaszewicz, & Mauguière, 1995; Michie, 1984; Michie et al., 1987).

Our findings that crossmodal ERP effects occurred under both attended and unattended conditions, and that such crossmodal modulations occurred earlier than attentional modulations may suggest that, at least under the present experimental circumstances, integration of visual-tactile stimuli may take place at a preattentive stage of processing. Likewise, previous behavioural as well as ERP studies looking at multisensory integration in other modalities than touch and vision have also suggested that multisensory integration may occur preattentively (e.g., Bertelson et al., 2000; Fort, Delpuech, Pernier, & Giard, 2002; Giard & Peronnet, 1999; McDonald, Teder-Salejarvi, & Ward, 2001; Vroomen et al., 2001). On the other hand, recent evidence has suggested that multisensory integration and attention may interact. For instance, Talsma & Woldorff (2005) showed that audio-visual integration effects on ERPs (i.e., superadditive responses) were larger in amplitude and occurred earlier when attention was directed to the site where visual and auditory stimuli were presented (i.e., attended trials); and in a later study Talsma et al. (2007) showed that superadditive effects depended on both visual and auditory modalities being attended. The heterogeneity of the results from the abovementioned studies suggests that the interplay between crossmodal integration and attention may be flexible and depend on experimental factors.

In the present study, a space x congruence x attention interaction, although absent for the P100 time interval, was found in the later N140 time range, indicating that attentional modulations (i.e., enhanced amplitudes for attended relative to unattended trials) were present for 'near-space-congruent' and 'far-space' trials (both '-congruent' and '-incongruent' trials) but failed to reach significance for 'near-space-incongruent' trials. Two considerations may be drawn from this result. First, we can speculate that in the 'near-space-incongruent' *attended* trials the visual stimuli, which are delivered on the (tactually-) unattended side, might act as exogenous cues (see Macaluso et al., 2000a, 2001) and draw attention away from the side of tactile stimulation. As a result, no attentional enhancement on ERPs would be present for the 'near-space-incongruent' *attended* trials, which therefore would not reliably differ from the 'near-space-incongruent' *unattended* trials. Second, the result that attentional ERP modulations were present when visual stimuli were delivered in far as well as in close space (at least for

'near-space-congruent' trials) indicates that effects of tactile spatial attention are not influenced by whether task-irrelevant visual stimuli were presented near or far from the body. This result is supported by the lack of a significant space x congruence x attention interaction for ERPs recorded at occipital electrode sites (which are likely to reflect mainly visual ERPs) in the time interval of the N140 component. These results together with our crucial finding of crossmodal spatial-congruence effects for 'near-space' trials, rule out the account that crossmodal effects in this study may be due to different attention distribution in radial (near vs. far) space; and are in favour of specific interaction effects between the two modalities. In summary, the findings from the current study provide ERP evidence in support of the spatial rule of multisensory integration between vision and touch in humans. That is, crossmodal visual-tactile interactions modulate somatosensory processing depending on the spatial relationship between visual and tactile stimuli, with enhancement of ERPs under conditions when visual stimuli are presented at the same location as tactile stimuli compared to conditions when visual stimuli are presented at a different location in peripersonal or extra-personal space. Importantly, crossmodal spatial effects have been found to occur irrespective of whether or not attention is directed to the site of tactile stimulation, and to precede attentional modulations.

3.5 Limitations of the study

Some potential caveats of the study presented in this chapter are discussed here. First, because the participants' fixation point was placed half-way between the location of the 'near' and 'far' visual stimuli, the visual angle under which visual stimuli were seen in the 'near-space' and 'far-space' trials was different, and as a result visual stimuli presented in near space fell in the lower visual field, while visual stimuli presented in far space were in the upper visual field. Because of the retinotopic organization of the visual cortex (V1), upper-field and lower-field visual stimuli are processed by discrete regions within V1 (Fox, Miezin, Allman, van Essen, & Raichle, 1987), and this may be reflected in differences between visual ERPs for visual stimuli presented in 'near-space' and 'far-space' trials, which in turn could affect crossmodal effects on ERPs. Similarly, the difference between retinal images of the visual stimuli in the 'near-space' and 'far-space' conditions (i.e, smaller in the latter condition, due to the greater spatial distance) may affect visual ERPs and possibly crossmodal ERP modulations. However, it should

be noted that (a) crossmodal spatial-congruence ERP effects were found in the 'near-space' but not in the 'far-space' condition, despite the fact that within each condition ('near-space' and 'far-space) the visual angle and size of retinal images were the same for 'congruent' and 'incongruent' trials; and (b) ERPs obtained in 'near-space-incongruent' and 'far-space' trials (both '-congruent' and '-incongruent') did not differ statistically. Taken together, these results suggest that differences in the visual angle under which visual stimuli were seen in the two conditions may not be crucial for the crossmodal spatial effects found in this study.

Another possible caveat could be that because in the present study the presentation of visual stimuli in near versus far space is blocked (and thus predictable), as a result spatial attention might be *divided* between near and far space in 'far-space' blocks, and *focused* within peripersonal space in 'near-space' blocks. This same potential confound is present in previous studies that manipulated the location of visual stimuli in near and far space (see, e.g., Ladavas et al., 1998). However, unlike these previous studies, the paradigm used in the present study allows us to control for this potential confound by comparing attentional modulations of ERPs obtained under conditions when visual stimuli are presented in near and far space. Crucially, these attentional effects were not found to differ between 'near-space' and 'far-space' trials, suggesting that the crossmodal spatial-congruence effects found in this study do not rely on differences in spatial allocation of attention.

Moreover, it could be argued that running a practice block in which participants had to respond to visual stimuli might have increased the relevance of task-irrelevant visual stimuli during the subsequent experimental blocks. Because in the experimental blocks visual stimuli were presented peripherally for a short time (200 ms), it was essential to ensure that these, although task-irrelevant, were perceived. Before the start of the experimental conditions, participants were given careful instructions to ignore visual stimuli throughout the experimental blocks. Several previous studies on crossmodal interactions and crossmodal spatial attention, have used paradigms in which different sensory modalities (e.g., vision and touch) were to be attended in different, alternating blocks while stimuli in the task-irrelevant modality for that given block had to be ignored (e.g., Eimer, 2001; Eimer & Driver, 2001; Talsma, Doty & Wolorff, 2007). That is, stimuli in one modality, (e.g., vision) were to be attended in one block, while they had to be ignored in the next block, and so on. Likewise, in the present study

visual stimuli were task-relevant and required a response in the practice block, while they had to be ignored during the two experimental conditions.

Another criticism that could be addressed is that we did not use a psychophysical method to assess whether the white noise was sufficiently loud to remove auditory cues produced every time that the tactile stimulators were activated. However, for all participants white noise was set at levels at which three expert people (not included in the sample) reported that they could no longer perceive any noise produced by the tactile stimulators.

Another consideration is that there is a delay between the onset of tactile stimulus and the actual contact between the rod and the skin, which has been estimated 5 ms. Because our main interest in all studies reported in this thesis is on tactile processing (i.e., ERPs recorded over and near somatosensory cortex), ERP waveforms in all studies have been shifted by 5 ms to align the intersection between the y- and x-axes with the actual start of tactile stimulation (skin contact).

Finally, the number of participants included in the sample of this study (twelve) is comparable to that used in the majority of ERP studies investigating sensory processes, and relies on the assumption that brain correlates of low-level processing do not vary greatly in neurologically unimpaired young adults.

Chapter 4

When far is near: ERP correlates of crossmodal spatial interactions between tactile and mirror-reflected visual stimuli

Visual-tactile interactions occur in a privileged way in peripersonal space, namely when visual and tactile stimuli are in spatial proximity. Here, we investigated whether crossmodal spatial-congruence effects (i.e., stronger crossmodal interactions for spatially congruent compared to incongruent visual and tactile stimuli) are also present when visual stimuli presented near the body are indirectly viewed in a mirror, that is, appearing in far space. Participants performed a tactile discrimination task while ignoring task-irrelevant visual stimuli presented simultaneously with tactile stimuli. Visual stimuli were delivered in peripersonal space either at congruent or incongruent locations as touch, and were observed either directly ('direct-viewing' condition) or as indirect mirror reflections ('mirror-viewing'condition). Crossmodal spatial modulations on ERPs recorded over and close to somatosensory cortex were found under both 'direct-viewing' and 'mirror-viewing' conditions; that is, ERPs were enhanced in response to tactile stimuli coupled with spatially congruent versus incongruent visual stimuli. However, while in the 'direct-viewing' condition spatial-congruence effects were present from 115 ms after the onset of visual and tactile stimuli, in the 'mirror-viewing' condition these effects only emerged around 190 ms after stimuli onset. These findings suggest that visual stimuli observed in a mirror are recoded as peripersonal stimuli, and furthermore that the remapping of mirror reflected visual stimuli as peripersonal ones may delay the integration of tactile inputs and mirror-reflected visual stimuli.

4.1 Introduction

Peripersonal space is the portion of space surrounding the body, and body parts (e.g., the hands), where we interact with (e.g., reach) objects in the environment (e.g., Rizzolatti, Fadiga, Fogassi, & Gallese, 1997). In everyday life, objects falling within

peripersonal space are normally perceived through more than one sensory modality, such as vision and touch. Accordingly, over the last few decades research from different disciplines has provided ever-growing evidence that the brain represents one's body and the space near the body in a multisensory fashion (see Fogassi, Gallese, Fadiga, Luppino, Matelli, & Rizzolatti, 1996; Holmes & Spence, 2004; Ladavas & Farne', 2004a). Neurophysiological research in animals has identified a network of cortical and subcortical brain areas, including the ventral premotor cortex, the posterior parietal cortex, the putamen, and the superior colliculus, that may subserve the visuo-tactile representation of peripersonal space (Avillac, Ben Hamed, & Duhamel, 2007; Bremmer, Schlack, Duhamel, Graf, & Fink, 2001; Duhamel, Colby, & Goldberg,, 1991, 1998; Fogassi et al., 1996; Graziano & Gross, 1993; Rizzolatti, Scandolara, Matelli, & Gentilucci, 1981). Specifically, a number of these neurophysiological studies (see Duhamel, Colby, & Goldberg, 1991, 1998; Graziano & Gross, 1993), as well as neuropsychological investigations in human participants (di Pellegrino, Làdavas, & Farnè, 1997; Làdavas, 2002; Làdavas & Farnè, 2004a; Làdavas, di Pellegrino, Farnè, & Zeloni, 1998), have shown that crossmodal interactions between touch and vision are stronger for visual stimuli in close proximity (i.e., within few centimeters) to the body part touched (e.g., peri-hand space), while crossmodal effects diminish when visual stimuli appear in far space (e.g., about 35 cm from the participant's hands ; see Làdavas et al., 1998). Taken together, these findings suggest that the visuo-tactile representation of peripersonal space may be neurally distinct from the representation of far extra-personal space.

However, recent research in humans and animals suggests that the brain's multimodal representation of the body and of peripersonal space is plastic and can be modulated to 'incorporate' regions of extrapersonal space that, e.g., become reachable by means of tools (see, e.g., Berti & Frassinetti, 2000; Iriki, Tanaka, & Iwamura, 1996). For example, a number of studies in healthy participants and in right-brain-damaged patients with neglect and/or tactile extinction have shown that crossmodal interactions between tactile stimuli delivered to the hands and simultaneous visual stimuli are stronger when the latter are presented at the tip of tools held by the participants compared to when these are presented at a comparable distance but are not associated with the tools (Farnè et al., 2005; Farnè & Làdavas, 2000; Pavani et al., 2000; Maravita et al., 2002; Maravita et al., 2001; Maravita, Spence, Kennett, & Driver, 2002a; Holmes, Calvert, & Spence, 2004). In line with these findings, the plasticity of representations of

visuo-tactile peripersonal space has also been shown with the use of mirrors. 'Mirror situations' are particularly interesting to investigate as they present a number of challenges to our brain. Firstly, in a mirror we see ourselves from an allocentric point of view, that is the view under which we commonly see other people, and as a result, e.g., the right hand looks like a left hand although it appears on the right side of space. Second, when we look at ourselves in a mirror, visual and proprioceptive inputs relative to our own body parts are in conflict, as we see our own body at a different location (i.e., in extrapersonal space) from where we feel it. Finally, and crucially, visual stimuli presented near the body and seen indirectly in a mirror project the retinal image of distant objects. Through extensive experience with mirrors in everyday life, humans have learned to recognize their own body parts in a mirror, and to correlate tactile sensations produced by an object (e.g., a comb through the hair) with the distant visual image of the object seen in a mirror. That is, we are fully aware of the true location of objects that we only see reflected in mirrors. Recent studies have suggested that visuo-tactile peripersonal space may be remapped to include mirror-reflected images of body parts, and the space around these, that appear in extra-personal space. Namely, these studies have shown that tactile stimuli can interact with visual stimuli that are observed at a distance via a mirror. For example, Maravita and colleagues (Maravita et al., 2000a) showed in a right-brain-damaged patient that detection of contralesional (left) touch was decreased by the presentation of a simultaneous, task-irrelevant visual stimulus near the ipsilesional hand (i.e., within few cm) (crossmodal extinction) when visual stimuli were observed indirectly as mirror-reflections compared to when these were presented in far space at a distance that produced a comparable retinal image as the mirror image. Similarly, using a crossmodal congruency task whereby participants had to judge the elevation of tactile stimuli delivered either to their index finger (up) or thumb (down) while ignoring visual distractors presented at congruent or incongruent locations to touch (see Pavani et al., 2000), Maravita and colleagues (Maravita, Spence, Sergent, & Driver, 2002b) showed that crossmodal interference by visual distractors on tactile elevation discriminations were more effective when visual distractors presented near the hands were observed via a mirror compared to conditions when visual distractors were presented at a distance from the hands in extra-personal space. Taken together, these results suggest that visual-tactile interactions are stronger under conditions when visual stimuli presented near the hands are seen in a mirror compared to conditions when these are presented in far space. This may indicate that visual stimuli observed via a mirror

are treated as near-the-body stimuli, according to their actual location (inferred by the knowledge of the properties of reflecting surfaces), rather than as distant stimuli as suggested by their retinal image (i.e., low-level physical processing); although a direct comparison between conditions when visual stimuli are seen directly near the hands and as mirror reflections has not been investigated by these previous studies. In sum, the findings above suggest that higher cognitive (top-down) mechanisms rather than bottom-up processing may be involved in perceiving the location of visual stimuli observed via a mirror for crossmodal integration. However, the neural correlates of this process were not addressed by previous studies.

Here, we investigated whether behavioural and electrophysiological responses to tactile stimuli coupled with visual stimuli are modulated by the actual spatial relationship between tactile and visual stimuli when the latter are observed via a mirror; the rationale being that spatially congruent visual and tactile stimuli should result in stronger crossmodal interactions compared to incongruent visual-tactile stimuli (Sambo & Forster, 2009; Macaluso, 2006; Macaluso & Driver, 2005; Làdavas & Farnè, 2004a; Avillac et al., 2007; Duhamel et al., 1998). Participants had to attend to one side of space in order to detect infrequent tactile target stimuli (stimuli with a 'gap') presented at the currently attended side (10% of total trials), while ignoring tactile targets presented at the unattended side (10%), any tactile non-targets (80%) (continuous stimulation), and any visual stimuli. The visual stimuli were presented simultaneously with tactile stimuli near one of the hands (i.e., in peripersonal space) either at congruent or incongruent locations as touch. Participants performed the task under two viewing conditions: in the 'direct-viewing' condition participants saw the visual stimuli directly near their hands, while in the 'mirror-viewing' condition the participants' hands and the visual stimuli were not directly visible, and could only be seen via a mirror. We predicted that if mirror reflections of visual stimuli are recoded as originating in peripersonal space, as previous neuropsychological and behavioural studies suggest (Maravita et al. 2000; Maravita et al. 2002b), ERPs and response speed to task-relevant tactile stimuli would be modulated by the actual spatial relationship between visual and tactile stimuli, reflected in an enhancement of ERP components and faster RTs to tactile stimuli presented with spatially congruent compared to incongruent visual stimuli, similar to what has been found for visual stimuli presented in peri-hand space and observed directly (see Chapter 3). Further, we predicted that if a remapping of visual stimuli as peripersonal stimuli in the mirror condition is mediated by higher cognitive

processes (i.e., prior experience and knowledge of reflecting surfaces), then this would not occur in a completely automatic fashion. As a result, top down influences from higher-order areas may be reflected in a delay in crossmodal spatial effects on ERPs in the 'mirror-viewing' condition. Alternatively, if mirror-reflected visual stimuli are treated as if they were distant objects in far extra-personal space (i.e., behind the mirror) as suggested by the retinal image that these project (i.e., bottom-up processing), no differences dependent on the actual spatial congruence of tactile stimuli and task-irrelevant visual stimuli would be present in behavioural and ERP responses (see Chapter 3 for ERP correlates of visual-tactile interactions when visual stimuli are presented in far space at a distance producing similar retinal images as the 'mirror' visual stimuli in the present study).

4.2 Methods

4.2.1 Participants

14 paid volunteers took part in the experiment. Two participants had to be excluded due to an excess of alpha waves. Thus, 12 participants (10 males and 2 females), aged between 21 and 37 years (average age: 28.5 years) remained in the sample. All participants were right-handed; and all had normal or corrected-to-normal vision by self-report. All participants gave their written informed consent. The study was approved by the Ethics Committee, City University London.

4.2.2 Stimuli and Apparatus

Participants sat in a sound-attenuated experimental chamber resting their arms on a table. Participants' index fingers were placed on top of two small boxes (3 x 5 x 3 cm) located on the table equidistant to the left and right of the participants' midline, at a distance of 40 cm from the participants' body. Each box had one tactile stimulator and one red LED (light-emitting diode) embedded in its surface, the LED being 1.5 cm distant from the tactile stimulator. Participants' index fingers were placed on top of each tactile stimulator at a distance of 40 cm from each other. In the 'mirror-viewing' condition, a 40 x 18 cm mirror was placed in front of the participants at the distance of 35 cm from the boxes, and centred relative to the participants' midline.

On each trial one tactile and one visual stimulus were presented simultaneously.

Tactile stimulation was provided using 12V solenoids driving a metal rod with a blunt conical tip to the top segment of the index finger making contact with the fingers whenever a current was passed through the solenoid. Tactile non-target stimuli consisted of one rod tip contacting participants' index finger for 200 ms. Tactile target stimuli were infrequent (i.e., 20% of total trials, overall), and had a gap of 4 ms in the continuous contact after a duration of 98 ms. Task-irrelevant visual stimuli were provided by 5 mm LEDs that were illuminated for 200 ms.

Each participant completed two experimental conditions: 'direct-viewing' and 'mirror-viewing'. In both experimental conditions the visual stimuli were presented close to the participants' hands, either at the same (congruent) or opposite (incongruent) location as tactile stimuli. However, while in the 'direct-viewing' condition participants could see their hands and the visual stimuli directly, in the 'mirror-viewing' condition the participants' hands, and thus the visual stimuli, were hidden from the participants' direct view by a wooden shield, and these could only be seen as indirect reflections in the mirror (i.e., projecting a visual image corresponding to that of an object placed in far space). In the 'direct-viewing' condition a fixation square (a small white square, 0.64 cm^2) was placed between the hands along the midline, equidistant to the right and left hand; in the 'mirror-viewing' condition the fixation square was placed on the centre of the mirror (see Fig. 4.1). This was done so that the fixation point was seen as located between the hands in both experimental conditions. White noise (50 dB, measured from the position of the participant's head) was presented from two loudspeakers placed at 110 cm from the participants' head and equidistant to the right and left of the midline, to mask any sound made by the tactile stimulators. Participants responded to target stimuli by pressing a button with either foot. Half of participants responded with their left foot and the other half with their right foot.

Experimental setup

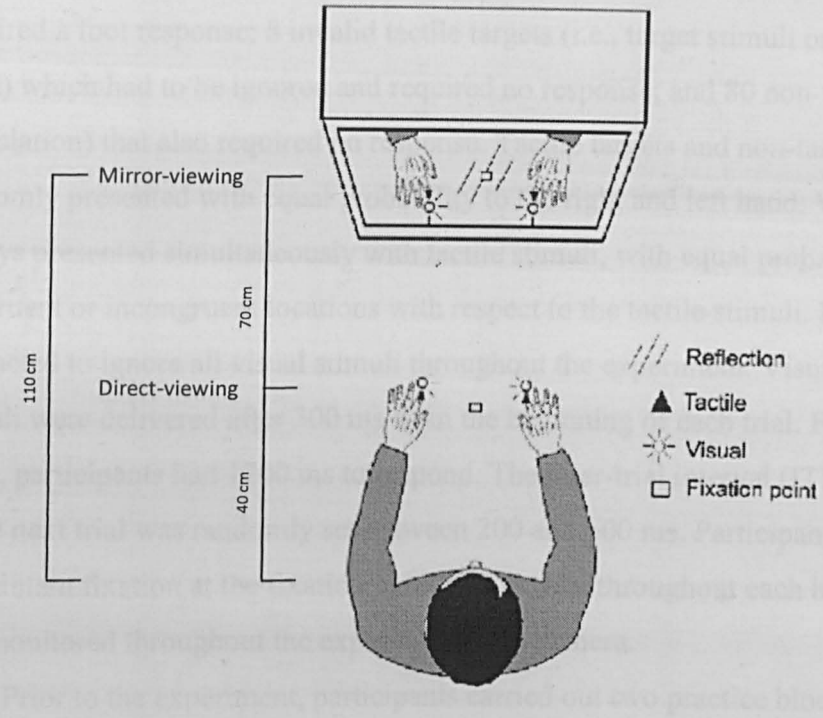


Figure 4.1 Schematic representation of the experimental setup showing the sites of tactile stimulation and the *apparent* locations of visual stimuli in the 'direct-viewing' and 'mirror-viewing' experimental conditions. In the 'mirror-viewing' condition, a mirror was placed at a distance of 35 cm from the participants' hands; due to mirror properties, this resulted in the visual stimuli appearing at a double distance (i.e., 70 cm) from the participants' hands. The actual distances of mirror-reflections from the hands (70 cm) and from the body (110 cm) are indicated on the left side of the figure. In the 'mirror-viewing' condition, the participants' hands were covered and were only visible as mirror reflections. The fixation point (a small square) was located at different locations in the two experimental conditions (the figure shows both locations). See text for further details.

4.2.3 Procedure

Each participant performed two experimental conditions: 'direct-viewing' and 'mirror-viewing'. Half of the participants performed the 'direct-viewing' condition first followed by the 'mirror-viewing' condition, for the other half this order was reversed. In each experimental condition, participants completed 12 experimental blocks of 96 trials each. In alternating blocks, they were instructed to attend either to their right or left

hand throughout the block in order to respond to infrequent tactile target stimuli ('gap' stimulation) at the attended hand[9]. Half of the participants attended to their right hand in the first block while the other half started with their left hand. Each block consisted of 8 valid tactile targets (i.e., tactile target stimuli delivered to the attended hand) which required a foot response; 8 invalid tactile targets (i.e., target stimuli on the unattended hand) which had to be ignored and required no response; and 80 non-targets (continuous stimulation) that also required no response. Tactile targets and non-targets were randomly presented with equal probability to the right and left hand. Visual stimuli were always presented simultaneously with tactile stimuli, with equal probability either at congruent or incongruent locations with respect to the tactile stimuli. Participants were instructed to ignore all visual stimuli throughout the experiment. Visual and tactile stimuli were delivered after 300 ms from the beginning of each trial. From the stimuli onset, participants had 1200 ms to respond. The inter-trial interval (ITI) before the start of the next trial was randomly set between 200 and 600 ms. Participants were instructed to maintain fixation at the fixation point (see above) throughout each block, and this was monitored throughout the experiment via a camera.

Prior to the experiment, participants carried out two practice blocks of 48 trials each to ensure that they could perceive the visual stimuli and discriminate the tactile stimuli. The first block consisted of only visual stimuli presented randomly and with equal probability near the right or the left hand. In one half of the block (24 trials) visual stimuli were observed under direct view, and in the other half (24 trials) these were observed under mirror view. The two halves of the block were separated by a short interval, and the order of the conditions under which visual stimuli were observed (i.e., direct and mirror view) was counterbalanced across participants. Participants had to respond to all visual stimuli. The second block consisted of only tactile stimuli; tactile target stimuli ('gap' stimulation) and tactile non-target stimuli (continuous stimulation) were delivered randomly in equal proportion and with equal probability to the right and the left hand. Participants had to respond to all tactile targets while ignoring tactile non-target stimuli. Participants started the experimental session only when their accuracy in the two practice blocks was 75% or above. The data of the pre-experimental blocks was not analyzed further. After completing the practice blocks and just before the start of the

[9] Tactile-spatial attention was manipulated with the purpose of making the location of tactile stimuli task-relevant, as previous studies (Forster et al., 2002; Gondan et al., 2005; Posner, 1978) have suggested that crossmodal spatial effects are less likely to be present when the spatial location of stimuli is task-irrelevant.

experiment, participants were given instructions to ignore visual stimuli throughout the experimental blocks.

4.2.4 Recording and Data Analysis

EEG (electroencephalogram) was recorded with Ag-AgCl electrodes from 28 scalp electrodes (midline electrodes: Fz, Fcz, Cz, Pz; electrodes over the right hemisphere: Fp2, F4, F8, Fc2, Fc6, C4, T8, Cp2, Cp6, P4, P8, O2 and the homologous electrode sites over the left hemisphere), using BrainVision recording system (BrainAmp amplifier and BrainVision Recorder software, version 1.02; Brain Products GmBH, Gilching, Germany; http://www.brainproducts.com). The amplifier bandpass was 0.01-100 Hz. Horizontal electrooculogram (HEOG) was recorded bipolarly from the outer canthi of both eyes. Electrode impedance was kept below 5 kΩ. EEG and EOG were sampled with a 500 Hz digitization rate, and, subsequently, were digitally filtered off-line with a 40 Hz low pass filter. EEG data were analyzed using BrainVision Analyzer software (version 1.05) (Brain Products GmBH, Gilching, Germany). EEG and EOG were epoched off-line into 700 ms periods, starting 100 ms before and ending 600 ms after the onset of tactile and visual stimuli. ERPs for tactile non-target stimuli coupled with task-irrelevant visual stimuli were averaged relative to a 100-ms pre-stimulus baseline. Trials with eye blinks (Fp1 or Fp2 exceeding ± 60 μV relative to baseline), horizontal movements (HEOG exceeding ± 30 μV relative to baseline) or other artifacts (a voltage exceeding ± 60 μV relative to baseline at electrodes Fc6, C4, Cp2, Cp6, P4, P8, T8 and at homologous electrode sites over the left hemisphere) measured within 600 ms after stimuli onset, were excluded from analysis. These represented approximately one-fourth of all trials in each single-subject average. Trials immediately following a response were also excluded from analysis in order to avoid contamination by movement-related artifacts (about 10% of the total trials on average). The total number of trials included in the analysis in each single-subject average ranged between 116 and 168 per each trial type (i.e., 'direct-viewing-congruent', 'direct-viewing-incongruent', 'mirror-viewing-congruent', 'mirror-viewing-incongruent'), including attended and unattended trials. Electrodes were remapped to ipsilateral and contralateral recording sites with respect to the hand where the tactile stimulus was delivered. To investigate effects of crossmodal spatial-congruence on processing within somatosensory cortex, ERPs recorded over and close to somatosensory cortex were compared for 'congruent' and 'incongruent' trials (i.e., spatially congruent vs.

incongruent visual and tactile stimuli) under attended and unattended conditions, for the 'direct-viewing' and 'mirror-viewing' experimental conditions. Based on earlier reports on crossmodal *spatial* effects, and on visual inspection of the ERP grand averages, ERP mean amplitudes were computed within the following measurement windows centred on the peak latencies of ERP components (Fig. 4.2 and 4.3): P100 component (85-114 ms after stimuli onset), N140 component (115-190 ms after stimuli onset), and N200 component (191-235 ms after stimuli onset). The subsequent time interval (236-300 ms after stimuli onset) was also included in the analysis. Statistical analysis (repeated measures ANOVAs) was conducted on ERP mean voltage for electrode sites over and near somatosensory cortex contralateral to the tactile stimulus location (i.e., Fc5/6c, C3/4c, T7/8c, Cp5/6c, P3/4c, and P7/8c), where crossmodal spatial-congruence effects were evident, as expected based on previous evidence from single-cell recordings in humans (see Duhamel et al., 1998) and neuroimaging and electrophysiological studies in humans (see Macaluso & Driver, 2005; Sambo & Forster, 2009). Separate ANOVAs were conducted for each of the time intervals indicated above, and included the factors viewing condition (direct- vs. mirror-viewing), congruence (congruent vs. incongruent), attention (attended vs. unattended), and electrode site (see above). To investigate crossmodal effects on response speed to tactile stimuli, a repeated measures ANOVA was performed on mean reaction times (RTs) to valid tactile target stimuli, with the factors viewing condition (direct vs. mirror viewing), congruence (congruent vs. incongruent) and target location (left vs. right).

4.3 Results

4.3.1 Behavioural data

Participants' response times (RTs) to infrequent valid tactile target stimuli[10] were on average 10.3 ms faster when task-irrelevant visual stimuli presented simultaneously with tactile stimuli were delivered at congruent compared to incongruent locations as touch (see Table 4.1). Overall statistical analysis comparing mean RTs to tactile targets on 'congruent' and 'incongruent' trials in the 'direct-viewing' and 'mirror-viewing' experimental conditions showed a main effect of congruence ($F_{[1, 11]} = 16.55$, $p < 0.003$), indicating faster RTs for 'congruent' compared to 'incongruent' trials. No

[10] For each participant, trials in which the RTs exceeded ±3 SD from the participant's average RTs were discarded. This procedure led to the removal of 2.7% of the trials overall.

interactions between the factors viewing condition (direct- and mirror-viewing) and congruence were obtained. Two follow-up ANOVAs, one for the 'direct-viewing' and one for the 'mirror-viewing' condition revealed a main effect of congruence in both experimental conditions ($F_{[1, 11]} = 13.44$, $p < 0.005$ for the 'direct-viewing' condition; and $F_{[1, 11]} = 7.77$, $p < 0.02$ for the 'mirror-viewing' condition), confirming that participants were faster at responding to tactile targets on 'congruent' compared to 'incongruent' trials under both 'direct-' and 'mirror-viewing' conditions. No other interactions involving the factor congruence were obtained in the overall analysis. There was no significant difference between the percentage of missed tactile targets between experimental conditions (Table 4.1), and the rate of false alarms to non-target stimuli was on average below 2 %.

Behavioural results (accuracy and mean RTs)

	Direct-viewing		**Mirror-viewing**	
	Congruent	**Incongruent**	**Congruent**	**Incongruent**
Missed responses	3.1%	3.9%	4.1%	3.8%
Mean RTs	248.1 ms	260.9ms	249.2.6 ms	257 ms

Table 4.1 Mean RTs and mean percentage of missed responses to tactile target stimuli under conditions when these were coupled with spatially congruent or incongruent task-irrelevant visual stimuli, in the 'direct-viewing' and 'mirror-viewing' experimental conditions.

4.3.2 Event-related brain potentials

Crossmodal spatial-congruence effects on ERPs recorded over and close to somatosensory cortex were determined by comparing ERPs obtained for tactile non-target stimuli coupled with spatially congruent vs. incongruent task-irrelevant visual stimuli under conditions when these were viewed directly near the hands ('direct-viewing' condition) and as indirect mirror reflections ('mirror-viewing' condition).

Figures 4.2 and 4.3 display effects of crossmodal visual-tactile interactions and tactile-spatial attention on grand-averaged ERPs elicited by tactile non-target stimuli coupled with spatially congruent (*solid lines*) vs. incongruent *(dashed lines)* visual stimuli, presented at tactually attended (*in black*) and unattended (*in grey*) locations, for the experimental conditions 'direct-viewing' and 'mirror-viewing', respectively. All

electrode sites included in the analysis (i.e., close to, and over somatosensory cortex; see above) are shown in the figures. Figure 4.4 shows overall crossmodal spatial modulations on ERPs in the 'direct-viewing' (*in black*) and 'mirror-viewing' (*in grey*) conditions collapsed across 'attended' and 'unattended' trials, at one of the electrodes (i.e., C3/4c; over somatosensory cortex).

As can be seen from Figure 4.2, under the 'direct-viewing' condition, tactile stimuli delivered at attended locations and coupled with spatially congruent visual stimuli (i.e., 'congruent-attended' trials) elicited enhanced ERPs compared to stimuli delivered under all the other trial types (i.e., 'incongruent-attended', and 'congruent-' and 'incongruent-unattended' trials) in the time range of the N140 component. By contrast, under the 'mirror-viewing' condition (Figure 4.3), enhanced amplitudes for tactile stimuli presented at attended locations and coupled with spatially congruent visual stimuli (i.e., 'congruent-attended' trials) are evident in the time interval of the subsequent N200 component. In addition, as can be seen from Figure 4.4, ERPs elicited in the 'direct viewing' condition were somewhat enhanced compared to ERPs elicited in the 'mirror viewing' condition for both spatially congruent and incongruent visuo-tactile stimuli in the time interval overlapping with the P100 and N140 components.

'Direct-viewing'

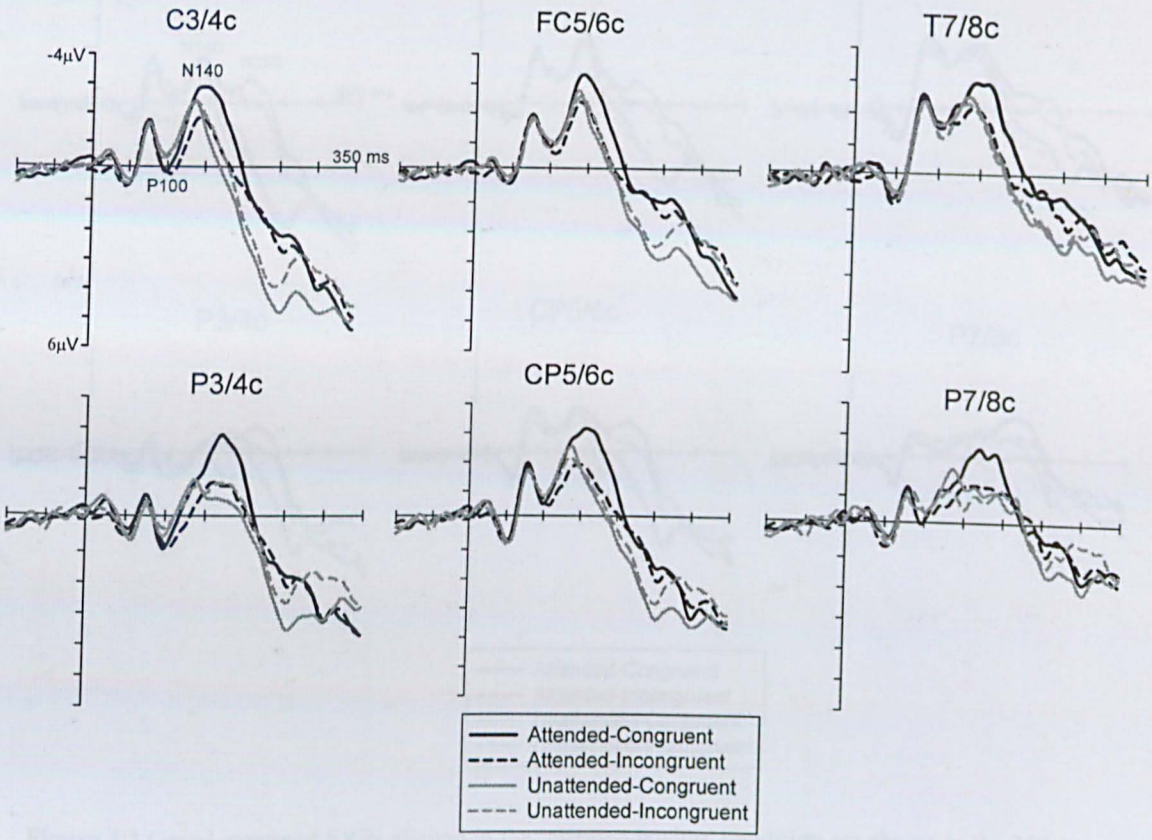


Figure 4.2 Grand-averaged ERPs elicited in the 'direct-viewing' condition in the 350-ms interval following stimuli onset by tactile non-target stimuli coupled with spatially 'congruent' (*solid lines*) and 'incongruent' (*dashed lines)* visual stimuli for 'attended' (*in black*) and 'unattended' (*in grey*) trials. ERPs are shown for electrodes contralateral to the site of tactile stimulation.

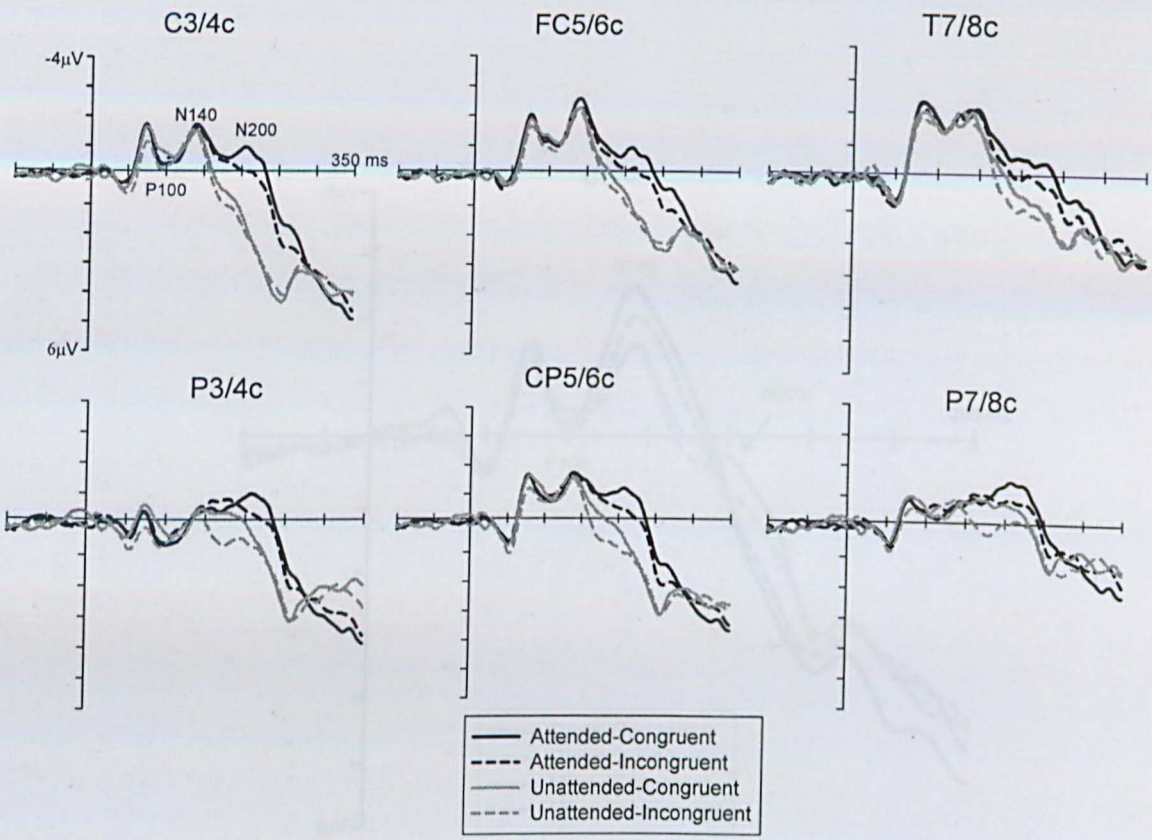


Figure 4.3 Grand-averaged ERPs elicited in the 'mirror-viewing' condition are shown in the 350-ms interval following stimuli onset by tactile non-target stimuli coupled with spatially 'congruent' (*solid lines*) and 'incongruent' (*dashed lines)* visual stimuli for 'attended' (*in black*) and 'unattended' (*in grey*) trials. ERPs are shown for electrodes contralateral to the site of tactile stimulation.

Crossmodal spatial-congruence effects

'Direct-viewing' and 'Mirror-viewing'

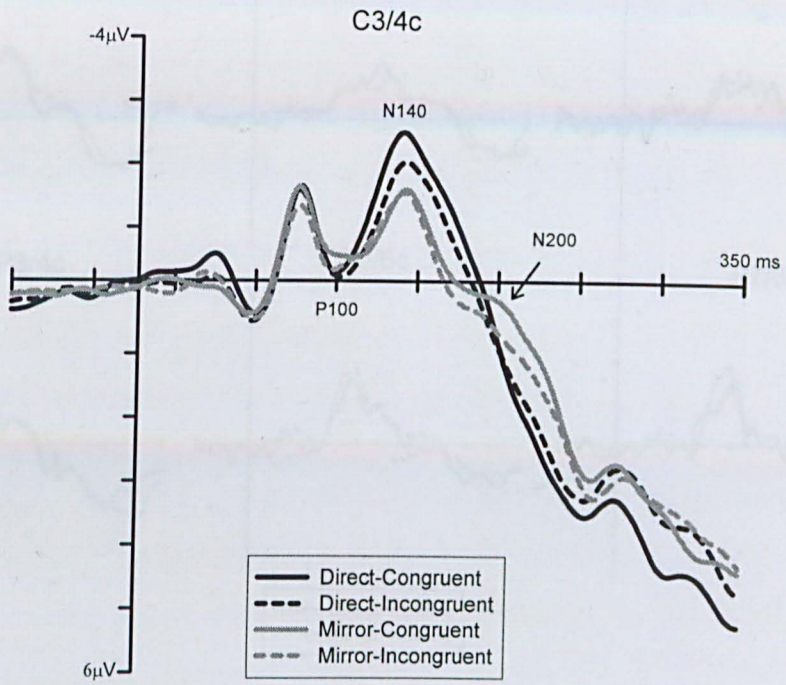


Figure 4.4 Grand-averaged ERPs elicited by tactile non-target stimuli coupled with spatially congruent (*solid lines*) vs. incongruent (*dashed lines*) visual stimuli in the 'direct-viewing' (*in black*) and 'mirror-viewing' (*in grey*) conditions, at one of the electrode sites included in the analysis (i.e., C3/4; over somatosensory cortex). Crossmodal spatial effects (i.e., enhancement of ERPs for spatially congruent vs. incongruent visual-tactile stimuli) can be observed at different time intervals under 'direct-' and 'mirror-viewing' conditions (see the Results section for details).

Finally, Figure 4.5 shows attentional modulations of ERPs; the figure displays difference ERP waveforms obtained by subtracting ERPs elicited in 'unattended' trials from ERPs elicited in 'attended' trials, separately for the 'direct-viewing' (*solid lines*) and the 'mirror-viewing' (*dashed lines*) condition. As can be seen from the figure, attentional modulations show a similar pattern in the two viewing conditions.

Attentional effects

Difference waveforms: 'Direct-viewing' and 'Mirror-viewing'

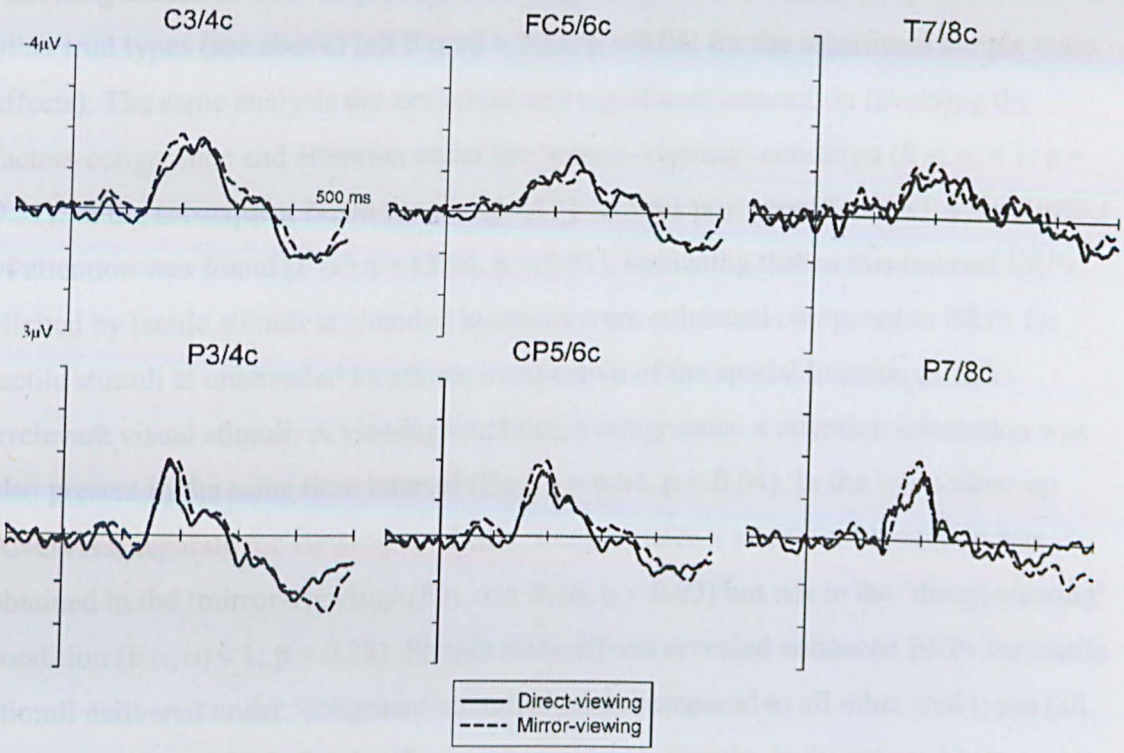


Figure 4.5 Difference ERP waveforms obtained subtracting ERPs elicited in response to non-target stimuli in 'unattended' trials from ERPs in the 'attended' trials in the 500-ms time interval following stimuli onset, separately for the 'direct-viewing' (*solid lines*) and the 'mirror-viewing' (*dashed lines*) conditions.

Statistical analysis (repeated measures ANOVAs) substantiated these observations. A significant main effect of viewing condition was present in the time range of the P100 (85-114 ms post-stimuli onset) and the N140 (115-190 ms post-stimuli onset) components ($F_{[1, 11]} = 4.32$, $p < 0.05$; $F_{[1, 11]} = 7.73$, $p < 0.02$, respectively), indicating that overall ERP amplitudes in these intervals were greater under the 'direct-viewing' compared to the 'mirror-viewing' condition. No other main effects or interactions were obtained in the time interval of the P100 component. In the subsequent N140 time range (115-190 ms post-stimuli onset), a main effect of attention was found, reflecting overall enhanced amplitudes for tactile stimuli delivered at attended compared to unattended locations, irrespective of the relative location of task-irrelevant visual stimuli ($F_{[1, 11]} = 7.35$, $p < 0.03$). A viewing condition x congruence x

attention interaction was also obtained in the same time range ($F_{[1, 11]} = 12.14$, $p < 0.01$). Two follow-up ANOVAs one for each viewing condition showed a congruence x attention interaction under the 'direct-viewing' condition ($F_{[1, 11]} = 5.13$, $p < 0.05$), reflecting enhanced ERP amplitudes for 'congruent-attended' trials compared to all other trial types (see above) (all $F_{[1, 11]} > 7.13$, $p < 0.05$; for the significant simple main effects). The same analysis did not reveal any significant interaction involving the factors congruence and attention under the 'mirror-viewing' condition ($F_{[1, 11]} < 1$; $p = 0.31$). In the subsequent N200 time range (191-235 ms post-stimuli onset), a main effect of attention was found ($F_{[1, 11]} = 13.26$, $p < 0.01$), indicating that in this interval ERPs elicited by tactile stimuli at attended locations were enhanced compared to ERPs for tactile stimuli at unattended locations, irrespective of the spatial location of task-irrelevant visual stimuli. A viewing condition x congruence x attention interaction was also present in the same time interval ($F_{[1, 11]} = 6.04$, $p < 0.04$). In the two follow-up ANOVAs, separate for viewing condition, a congruence x attention interaction was obtained in the 'mirror-viewing' ($F_{[1, 11]} = 8.16$, $p < 0.03$) but not in the 'direct-viewing' condition ($F_{[1, 11]} < 1$; $p = 0.28$). Simple main effects revealed enhanced ERPs for tactile stimuli delivered under 'congruent-attended' trials compared to all other trial types (all $F_{[1, 11]} \geq 5.83$, $p < 0.05$; for significant comparisons). Finally, in the interval between 236 and 300 ms after stimuli onset, a main effect of viewing condition was obtained ($F_{[1, 11]} = 9.22$, $p < 0.02$), indicating that in this interval ERPs were enhanced for the 'mirror-viewing' compared to the 'direct-viewing' condition. In addition, a main effect of attention was also found ($F_{[1, 11]} = 14.32$, $p < 0.01$), reflecting an enhanced sustained negativity for tactile stimuli presented at attended compared to unattended locations, irrespective of the relative location of visual stimuli. The interaction between viewing condition and attention was not significant ($F_{[1, 11]} = 1.78$, $p = 0.37$), indicating that attention modulations in this time interval were present under both 'direct-' and 'mirror-viewing' conditions.

4.4 Discussion

There is a substantial body of evidence showing that crossmodal interactions are stronger for spatially congruent compared to incongruent visual and tactile stimuli; that is, when visual stimuli are presented in peripersonal space near the stimulated body part

(e.g., peri-hand space) (Duhamel et al., 1998; Fogassi et al., 1996; Graziano & Gross, 1993; Làdavas, 2002; Sambo & Forster, 2009). Here, we provided behavioural as well as neural (ERP) evidence that crossmodal spatial-congruence effects between vision and touch can also occur when visual stimuli presented in peripersonal space are observed indirectly in a mirror, although under this condition the retinal image is consistent with stimuli being presented in far space. Participants' task was to detect tactile target stimuli (stimulation with a 'gap') at the attended hand (indicated at the beginning of each block) and to ignore tactile targets at the unattended hand, all tactile non-target stimuli (continuous stimulation), and any visual stimuli. Visual stimuli were task-irrelevant, and were presented simultaneously with tactile stimuli near the hands either at congruent or incongruent locations as touch. In separate blocks of trials, the visual stimuli were observed under two different viewing conditions; namely, directly near the hands ('direct-viewing' condition) and indirectly as distant mirror reflections ('mirror-viewing' condition). We found that participants' reaction times to tactile target stimuli were modulated by spatial congruence of visual and tactile stimuli; that is, responses were faster for tactile targets presented with spatially congruent compared to incongruent visual stimuli both when the visual stimuli were observed directly near the hands and when these were viewed indirectly near the mirror reflection of the hands. In line with these behavioural results, ERPs recorded over and near somatosensory cortex were enhanced for tactile stimuli coupled with spatially congruent compared to incongruent visual stimuli under both 'direct-viewing' and 'mirror-viewing' conditions. These crossmodal spatial effects were found to be present over the hemisphere contralateral to the site of tactile stimulation, in line with previous neuroimaging and electrophysiological studies in humans (see Macaluso & Driver, 2005; Sambo & Forster, 2009), as well as with the finding from single-cell recordings in animals that the receptive fields (RFs) of the majority of bimodal neurons are contralateral and require spatial congruence between tactile and visual stimuli (Duhamel et al., 1998). Notably, under direct vision of the hands (and of the visual stimuli) enhanced ERP amplitudes for spatially congruent visuo-tactile stimuli were found from 115 ms after onset of stimuli (i.e., overlapping with the N140 component), while under the 'mirror viewing' condition crossmodal spatial modulations were only observed from around 190 ms after stimuli onset (i.e., overlapping with the N200 component). That is, under the 'mirror-viewing' condition crossmodal spatial-congruence effects were delayed compared to the 'direct-viewing' condition. In addition, these crossmodal ERP effects were modulated

by spatial attention in both viewing conditions. Namely, crossmodal spatial effects were present under conditions when attention was directed to the site of tactile stimulation, but not when attention was directed to the opposite side of space.

The main finding that crossmodal spatial-congruence effects are present in a 'mirror situation' indicates that when the hands are only seen in a mirror, visual stimuli presented near the hands are not treated in accordance to their physical properties, that is, as originating in far space (i.e, in a bottom-up manner), but as peripersonal stimuli, on the base of previous knowledge and experience with mirror-reflecting surfaces (i.e., top-down processing). Indeed, if the true spatial source of visual stimuli was not computed by the brain, and these were coded as far stimuli as suggested by their retinal projections, then we would expect no modulations of ERPs by spatial congruence between tactile and visual stimuli when the latter are viewed in the mirror. That is, no differences should be present between ERPs for tactile stimuli coupled with visual stimuli presented in the same (congruent) and opposite (incongruent) hemispace as touch, as it has been shown to be the case when visual stimuli are actually presented in far space (see Chapter 3). Previous behavioural as well as neuropsychological studies also suggest that mirror-reflected visual stimuli may be remapped in terms of their actual spatial location near the body. These previous findings show that crossmodal effects between vision and touch are stronger when visual stimuli presented near the hands are seen as mirror reflections compared to conditions in which visual stimuli are presented in far space next to a rubber hand (Maravita et al., 2000; Maravita et al., 2002a). However, these studies only provide indirect evidence of a spatial remapping of mirror reflected visual stimuli as peripersonal stimuli, since no direct comparison between mirror and near-space conditions was made. The findings from the present study confirm and extend the results from the abovementioned studies by providing neural evidence in humans that crossmodal spatial-congruence effects can occur when visual stimuli appear in far space although these are presented in peripersonal space due to observation via a mirror.

The findings from this study are also in agreement with a neurophysiological study in macaque monkeys in which single-cell activity in response to visuo-tactile stimulation was recorded from the intraparietal sulcus (IPS) contralateral to the monkeys' stimulated hands (Iriki, Tanaka, Obayashi, & Iwamura, 2001). In this study, a proportion of the bimodal visuo-tactile neurons that responded to a visual probe in proximity to the somatosensory receptive fields (RFs) under direct vision of the hands

were also found to respond when the probe was positioned around the hand but the monkeys could only see their hands in a video monitor. Iriki and colleagues suggest that the visual RFs of these bimodal neurons were '*projected onto the video screen*' so that peripersonal space would incorporate the region of space around the image of the hand in the screen. However, the remapping of visual RFs only occurred after extensive training, during which the monkeys learned to recognize the image of their own hands in the monitor through active movements that required relying on visual information. In contrast, in the present study, task-irrelevant visual stimuli observed in a mirror appear to activate the representation of the region of space around the mirror-image of the hand without any training. In humans, higher-level cognitive factors (i.e., previous knowledge of the nature of reflecting surfaces) may mediate the activation of the representation of the space around the hand in mirror situations, as humans acquire familiarity with mirror properties through everyday experience with mirrors. Interestingly, however, the result from our study that in the 'mirror-viewing' condition crossmodal spatial modulations were present at later stages of processing than under the 'direct-viewing' condition may suggest that a spatial remapping of mirror-reflected visual stimuli according to their true external location requires additional time, and this, in turn, may somewhat delay the integration between visual and tactile stimuli at a neural level.

The result from the present study that crossmodal spatial-congruence effects between vision and touch are dependent on whether or not attention is directed to the site of task-relevant tactile stimulation is in line with some previous evidence showing that spatial attention modulates multisensory (audio-visual) integration processing (see Talsma & Woldorff, 2005; Talsma, Doty, & Woldorff, 2007). By contrast, other studies have shown that crossmodal integration may occur pre-attentively (Bertelson, Vroomen, De Gelder, & Driver, 2000; Foxe, Morocz, Murray, Higgings, Javitt, & Schroeder, 2000; Giard & Peronnet, 1999; Molholm, Ritter, Murray, Javitt, Schroeder, & Foxe, 2002). Talsma and Woldorff (2005) suggest that differences in experimental factors (e.g., stimuli eccentricity) could be responsible for the discrepant results on the role of attention in multisensory processing found in their study compared to other ERP studies. In particular, they argue that a stronger engagement of attention on the required location as a result of experimental procedures (see Talsma & Woldorff, 2005) could have determined both an enhancement of the attention effects on multisensory integration, and a slight delay (about 50 ms) of the integration process (see also Talsma

et al., 2007). Likewise, in the current study we found that spatial attention had a greater impact in modulating crossmodal spatial interactions than in our previous study (see Chapter 3) under conditions where visual stimuli were also presented in near space. That is, in our previous study crossmodal (visuo-tactile) spatial interactions were found to modulate ERPs over and near somatosensory cortex in the range of the P100 component irrespective of whether attention was directed or not to the site of tactile stimulation, while an attention x spatial congruence interaction was found in the range of the N140 component. On the other hand, in the present study the P100 component was not modulated by spatial congruence between visual and tactile stimuli, and the N140 component reflected crossmodal spatial effects only in trials where attention was directed to the site of touch, but not in the (tactually) unattended trials. One difference between the two studies that may have contributed to these somewhat discrepant results is that in the present study participants' gaze was directed in peripersonal space between their hands, while in our previous study the participants' gaze was directed in far extra-personal space. As a result, in the present study participants' attention may have been more strongly focussed in peripersonal space, and specifically to the site of the currently attended tactile stimulation, which could explain the attentional modulation of crossmodal effects. In addition, in the current study the lighting level of the experimental chamber was greater than in our previous study to allow participants to see their hands in the mirror. As a result, the visual stimuli appeared less bright, which could be responsible for the slight delay (in the order of a few tens of milliseconds) of the integration effects found in this study compared to our previous study in the conditions where visual stimuli were presented and directly observed in peripersonal space.

One could argue that the effect of visual stimuli on crossmodal spatial interactions in the present study might reflect (stimulus-driven) shifts of spatial attention rather than purely multisensory integration processes (see McDonald et al., 2000; Macaluso, Frith & Driver, 2000 for a full explanation of the two accounts). However, as Macaluso and colleagues argue, crossmodal integration and crossmodal spatial attention may be two aspects of the same process, whereby stimulation in one modality can spatially affect responses to another modality, and may involve the same neural circuitry (see Macaluso, Frith & Driver, 2000).

In addition to the spatial congruence effects discussed above, a main effect of attention was also obtained in the time range of the N140 and N200 components,

followed by a sustained negativity (236-300 ms after stimuli onset), reflecting enhanced amplitudes for stimuli presented at (tactually) attended compared to unattended locations. These attentional modulations are in line with previous ERP findings on tactile spatial attention (e.g., Eimer & Forster, 2003; Forster & Eimer, 2004, 2005). Furthermore, an enhancement of ERPs was obtained in the time range of the P100 and N140 components for stimuli presented under 'direct-viewing' compared to 'mirror-viewing' conditions, reflecting a main effect of viewing condition. This result may suggest that seeing one's own body parts (i.e., the hands) directly enhances ERP responses to visual and tactile events presented near the body (i.e., in peri-hand space), compared to when the hands are viewed as distant mirror reflections, regardless of spatial congruence between visual and tactile inputs. This finding may relate to previous reports showing that viewing the body enhances tactile processing (Kennett et al., 2001b; Press et al., 2004; Taylor-Clarke et al., 2002), although in these studies participants' gaze was always directed to the stimulated body part while in the present study participants maintained central fixation.

In conclusion this study provides the first neural evidence in humans for crossmodal spatial-congruence effects between vision and touch when (task-irrelevant) visual stimuli appear as distant mirror reflections although these are actually presented near the hands. That is, in the 'mirror-viewing' condition ERPs were enhanced, and RTs were faster, when visual stimuli were presented near the site of tactile stimulation compared to when these were presented at incongruent locations. Similar effects were obtained when the visual stimuli were observed directly near the hands. However, under the 'mirror-viewing' condition crossmodal spatial modulations of ERPs occurred at later time intervals compared to when the visual stimuli were seen near the hands. Overall, the findings from the present study suggest that visuo-tactile spatial-congruence effects may be also observed for visual stimuli that according to their retinal projections appear as distant ones, once far (mirror) space is remapped as near. This spatial remapping may be driven by higher cognitive factors, namely previous experience with mirror properties, and may delay the integration process of visual and tactile stimuli. Furthermore, we could speculate that the spatial remapping of mirror-reflected visual stimuli might involve the posterior parietal cortex, and more specifically the intraparietal sulcus, a brain region implicated in spatial representation across modalities which in monkeys has been also reported to respond to visuo-tactile stimuli when the visual stimuli were viewed indirectly in a video monitor (see Iriki et al., 2001).

4.5 Limitations of the study

Some possible limitations of the the study presented in this chapter are discussed in this section[11]. In particular, a few differences in the setup of the 'direct-' and 'mirror-viewing' conditions may be a potential confound and need to be addressed when interpreting the results of this study. First, the visual stimuli observed via a mirror are somewhat dimmer and project a smaller retinal image compared to the visual stimuli observed directly near the hands; and the same applies to the image of the hands reflected in a mirror. These differences could be responsible for the reduced amplitudes of the ERPs obtained in the 'mirror-viewing' condition compared to the 'direct-viewing' condition. Along similar lines, differences in the physical properties of the visual stimuli in the two viewing conditions, rather than higher-level processes alone, could possibly account for the the delay of crossmodal spatial-congruence effects in the 'mirror-' compared to the 'direct-viewing' condition.

Second, the two viewing conditions differed about the location of visual stimuli with respect to the locus of spatial attention. Namely, in the 'direct-viewing' condition visual stimuli presented at the (tactually) attended side were within the focus of spatial attention (i.e., near the body), while this may not be the case for the 'mirror-viewing' condition where visual stimuli are viewed at some distance from the body. As a result, task-irrelevant visual stimuli could be more salient and more strongly associated to tactile stimuli in the 'direct-' than in the 'mirror-viewing' condition, and this could be partly responsible for the delay of crossmodal spatial-conguence effects in the 'mirror-viewing' compared to the 'direct-viewing' condition.

Third, the choice of having a fixation point between the participants' hands in both viewing conditions resulted in the fixation point being placed at different locations in the two viewing conditions. Namely, in the 'direct-viewing' condition the fixation point was placed along the body midline, whereas in the 'mirror-viewing' condition this was located on the mirror. In the latter condition, the fixation point was thus at a different depth with respect to the visual images of the hands and the visual stimuli. This may have produced double images of the hands and of the visual stimuli visible in the mirror, which might be responsible for some of the differences between ERPs elicited in the two viewing conditions.

[11] For a discussion of more general limitations of the paradigm used in the studies presented in this and in the previous chapter, the reader should refer to section 3.5 of this thesis.

4.6 Comparison between 'mirror-viewing' and 'far-space' conditions

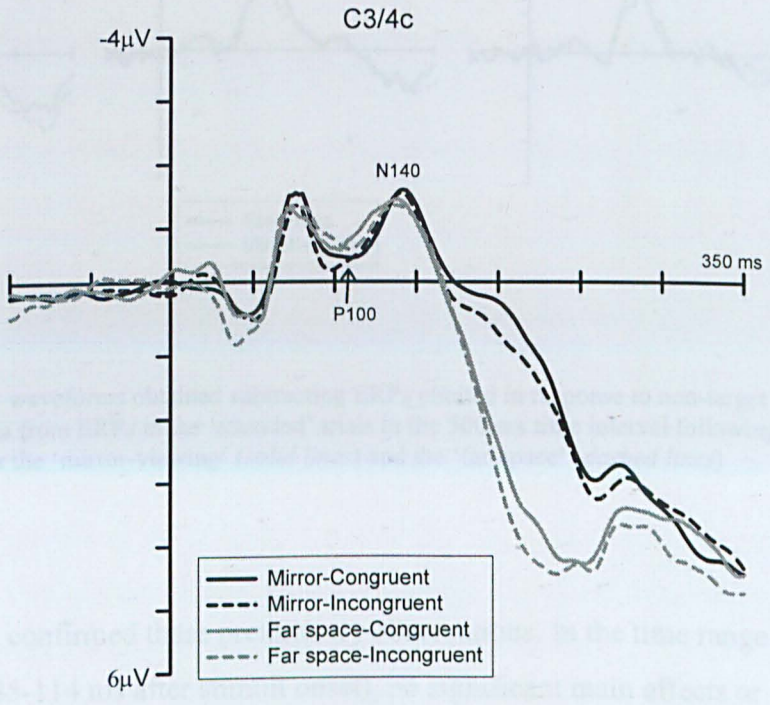
Some of the criticisms outlined above may be addressed by comparing ERPs obtained under conditions when task-irrelevant visual stimuli (presented near the hands) are observed in a mirror, and when these are presented in far space at a distance that produces comparable retinal images. That is, because these two conditions are comparable with respect to low-level properties of visual stimuli, as well as to the distribution of spatial attention, any differences between ERPs obtained under these conditions should be ascribed to a higher-level 'interpretation' of the actual location of visual stimuli with respect to tactile stimuli in the 'mirror-viewing' condition.

In the present study, a 'far-space' condition was not included for practical reasons (e.g., excessive number of trials for one session, learning effects, etc.); therefore a comparison between those two conditions cannot be achieved within the same group of subjects. In the study presented in Chapter 3, a 'far-space' condition was run using a similar apparatus and paradigm as that used in the 'mirror-viewing' condition described in this chapter. Importantly, because the distance of the visual stimuli from the participants' hands in the 'far-space' condition was twice the distance between the mirror and the participants' hands in the 'mirror-viewing' condition (i.e., 70 cm and 35 cm respectively), the retinal projections of visual stimuli in these two conditions are comparable.

Thus, a between-subjects ANOVA was performed between ERPs obtained in the 'mirror-viewing' and 'far-space' conditions with the same time windows and factors used in the ANOVA performed in the study presented in this chapter, with the addition of the factor 'condition' ('mirror-viewing' vs. 'far-space')[12]. Separate ERP waveforms for each of these two conditions can be found in the relevant sections of this thesis (3.3.2 for the 'far-space' condition, and 4.3.2 for the 'mirror-viewing' condition). Figure 4.6 in this section illustrates overall crossmodal spatial-congruence effects on ERPs in the 'mirror-viewing' (*in black*) and 'far-space' (*in grey*) conditions collapsed across 'attended' and 'unattended' trials, at one of the electrodes (i.e., C3/4c; over somatosensory cortex). As can be seen from the figure, ERPs elicited in the 'mirror-viewing' condition show a crossmodal spatial-congruence modulation around 200 ms post-stimuli (overlapping with the N200 component) which is not present in the ERPs

[12] This was chosen since no main effect of 'congruence' or interactions involving this factor were obtained in any of the time windows tested in the analysis performed in the study presented in Chapter 3 (see section 3.3), suggesting a lack of significant crossmodal spatial-congruence effects in this condition.

elicited in the 'far-space' condition. In addition, in the same time range, as well as at later latencies, ERPs in the 'mirror-viewing' condition appear generally enhanced compared to ERPs in the 'far-space' condition. Finally, as shown in the difference ERP waveforms in Fig. 4.7, attentional modulations were present in both conditions at similar latencies.



Attentional effects

Difference waveforms: 'Mirror-viewing'and 'Far-space'

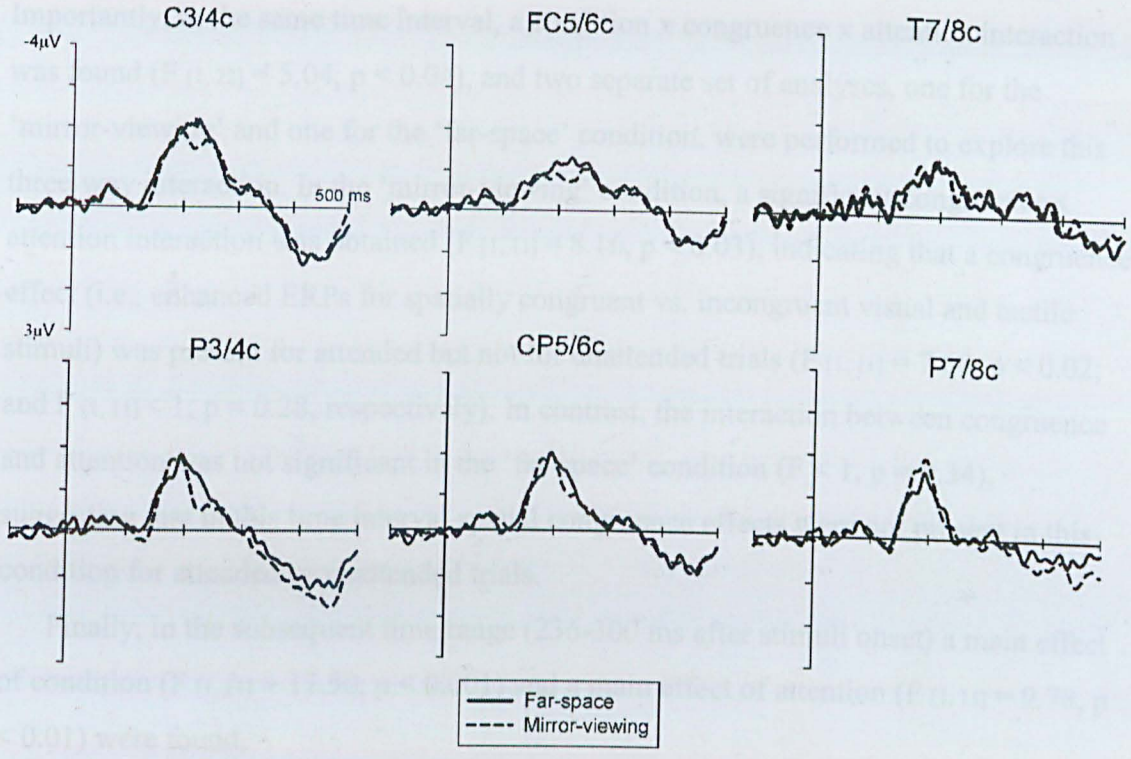


Figure 4.7 Difference ERP waveforms obtained subtracting ERPs elicited in response to non-target stimuli in 'unattended' trials from ERPs in the 'attended' trials in the 500-ms time interval following stimuli onset, separately for the 'mirror-viewing' (*solid lines*) and the 'far-space' (*dashed lines*) conditions.

Statistical analyses confirmed these preliminary observations. In the time range of the P100 component (85-114 ms after stimuli onset), no significant main effects or interactions between any of the factors were found. In the subsequent time interval, overlapping with the N140 component (115-190 ms after stimuli onset), a main effect of attention was obtained ($F_{[1, 22]} = 7.603$, $p < 0.02$), indicating that overall ERPs were enhanced for attended compared to unattended trials in this time interval. The interaction between attention and condition was not significant ($F < 1$, $p = 0.36$), indicating that in this time interval attentional effects in the two conditions did not differ significantly.

In the time interval of the N200 component (191-235 ms after stimuli onset), a main effect of the factor condition was found ($F_{[1, 22]} = 16.98$, $p < 0.001$), indicating

enhanced amplitudes in the 'mirror-viewing' condition compared to the 'far-condition'. A main effect of attention was also obtained in this time interval ($F_{[1,22]} = 10.535$, $p < 0.005$), reflecting enhanced amplitudes for attended compared to unattended trials. Importantly, in the same time interval, a condition x congruence x attention interaction was found ($F_{[1,22]} = 5.04$, $p < 0.04$), and two separate set of analyses, one for the 'mirror-viewing' and one for the 'far-space' condition, were performed to explore this three-way interaction. In the 'mirror-viewing' condition, a significant congruence x attention interaction was obtained ($F_{[1,11]} = 8.16$, $p < 0.03$), indicating that a congruence effect (i.e., enhanced ERPs for spatially congruent vs. incongruent visual and tactile stimuli) was present for attended but not for unattended trials ($F_{[1,11]} = 7.60$, $p < 0.02$; and $F_{[1,11]} < 1$; $p = 0.28$, respectively). In contrast, the interaction between congruence and attention was not significant in the 'far-space' condition ($F < 1$, $p = 0.34$), suggesting that in this time interval spatial congruence effects were not present in this condition for attended or unattended trials.

Finally, in the subsequent time range (236-300 ms after stimuli onset) a main effect of condition ($F_{[1,11]} = 17.50$, $p < 0.001$) and a main effect of attention ($F_{[1,11]} = 9.78$, $p < 0.01$) were found.

To summarize the results of the analysis reported above, crossmodal spatial-congruence effects between vision and touch were present when task-irrelevant visual stimuli were presented near the hands and observed in the 'mirror' space but not when these were presented in far space, although these two conditions are comparable for physical (low-level) properties of the stimuli. Furthermore, attentional modulations did not differ significantly between the 'mirror-viewing' and the 'far-space' conditions, suggesting that the distribution of spatial attention was comparable in these conditions. While offering a better control for low-level and attentional factors, these results confirm the findings presented in the main analysis in this chapter, and suggest that visual stimuli presented near the hands and indirectly observed in a mirror are treated as peripersonal stimuli, according to their *known* rather than to their *perceived* location. This argument will be further discussed in Chapter 7 (section 7.2.2).

Chapter 5

Viewing the body modulates neural mechanisms underlying sustained spatial attention in touch

Crossmodal links between vision and touch have been extensively shown with a variety of paradigms. The present ERP study aimed to clarify whether neural mechanisms underlying sustained tactile-spatial attention may be modulated by visual input, and the sight of the stimulated body part (i.e., the hands) in particular. Participants covertly attended to one of their hands throughout a block to detect infrequent tactile target stimuli at that hand while ignoring tactile targets at the unattended hand, and all tactile non-targets. In different blocks, participants performed this task under three viewing conditions: full vision, hands covered from view, and blindfolded. When the participants' hands were visible attention was found to modulate somatosensory ERPs at early latencies (i.e., in the time range of the somatosensory P100 and the N140 components), as well as at later time intervals (from 200 ms after stimulus onset). By contrast, when participants were blindfolded and, crucially, even when only their hands were not visible, attentional modulations were found to arise only at later intervals (i.e., from 200 ms post-stimulus), while earlier somatosensory components were not affected by spatial attention. The behavioural results tallied with these electrophysiological findings, showing faster response times to tactile targets under the full vision condition compared to conditions when participants' hands were covered, and when participants were blindfolded. The results from this study provide the first evidence of the impact of vision on mechanisms underlying sustained tactile-spatial attention which is enhanced by the sight of the body part (i.e., the hands).

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5.1 Introduction

When we expect to receive a touch on a certain part of our body, we may focus attention on that location, and we may also feel compelled to look at this body part. Covertly directing attention to a location on the body enhances tactile perception at that location (see e.g., Johansen-Berg & Lloyd, 2000; and Spence & Gallace, 2007 for reviews). Likewise, increasing evidence has shown that also viewing one's own body improves tactile detection and discrimination in healthy subjects (e.g., Tipper et al., 1998; Kennett et al., 2001b; Press et al., 2004) and in brain-damaged patients with somatosensory deficits (Serino et al., 2007), as well as it enhances cortical tactile processing (Taylor-Clarke et al., 2002). Furthermore, one PET (Positron Emission Tomography) study has shown that vision can modulate mechanisms underlying sustained covert spatial attention in touch (Macaluso et al., 2000b). Macaluso and colleagues reported that when participants had their eyes open, and their hands were visible throughout the task, covertly attending to one of their hands resulted in greater activity within the postcentral gyrus, corresponding to secondary somatosensory cortex (SI), and within the intraparietal sulcus (IPS), a region involved in spatial representation across modalities, in response to tactile stimuli delivered to that hand compared to the other, unattended, hand. By contrast, when participants performed the tactile task with their eyes closed, attentional modulations were only present within SI, but not in the IPS. This finding suggests that the IPS may be involved in the visual modulation of covert tactile-spatial attention, in line with the view that the highly accurate spatial information vision provides (Eimer, 2004; Warren, 1970) may facilitate the spatial selection of tactile locations. From Macaluso et al.'s (2000b) study it is not clear, however, whether it is ambient visual-spatial information or, specifically, the sight of the stimulated body parts (i.e., the hands) that plays a crucial role in modulating sustained tactile-spatial attention.

The present study was designed to investigate systematically whether different levels of visual input, namely ambient visual-spatial information (i.e., visual information about the environment or "structured visual field"; van Beers et al., 1999, p. 44) and vision of the hands, influence spatial attentional modulations at different stages of somatosensory processing. Electrophysiological studies have consistently reported that sustained tactile-spatial attention modulates somatosensory event-related potentials (ERPs) from early latencies, with greater ERP amplitudes for tactile stimuli at attended

relative to unattended locations (e.g., Eimer & Forster, 2003a; Zopf, Giabbiconi, Gruber, & Müller, 2004). However, no previous ERP study has investigated at which stages of processing the mechanisms underlying covert spatial attention in touch can be modulated by vision.

If vision helps tactile attentional selection, as we can hypothesize based on the finding that a crossmodal area (IPS) is recruited during tactile selection (in addition to modality-specific somatosensory areas) when participants have their eyes open compared to closed (Macaluso et al., 2000b), then we would expect attentional modulations of somatosensory ERPs to be greater and/or occur earlier when visual-spatial information and vision of the hands are available to observers than in the absence of visual input (that is, when participants are blindfolded), possibly as a result of top-down modulations from crossmodal associative areas to modality-specific areas. Moreover, we expected that attentional modulations would occur earlier under conditions when participants' hands are visible compared to when these are hidden from view, if vision of the hands has a specific role in modulating attentional effects during tactile spatial selection.

5.2 Materials and Methods

5.2.1 Participants

Fifteen paid volunteers took part in the experiment. Three had to be excluded for an excess of alpha waves. Thus, 12 participants (5 males and 7 females), aged between 21 and 38 years (average age: 28.4 years) remained in the sample. All participants were right-handed; and all had normal or corrected-to-normal vision by self-report. All participants gave their written informed consent prior to testing. The experiment was approved by the Ethics Committee, City University London; and was conducted in accordance with the Declaration of Helsinki.

5.2.2 Apparatus and Procedure

Participants sat in a dimly lit, sound-attenuated experimental chamber. Two small boxes (3 x 5x 3 cm), each having one tactile stimulator embedded in its surface, were located on a table in front of the participants, at a distance of about 40 cm from the participants' body. Participants' index fingers were placed on top of each tactile stimulator at a distance of 40 cm from each other, equidistant to the left and right of the

participants' midline.

On each trial one tactile stimulus was delivered; tactile stimulation was provided using 12V solenoids driving a metal rod with a blunt conical tip to the top segment of the index finger making contact with the finger whenever a current was passed through the solenoid. Tactile non-target stimuli consisted of the rod contacting the participants' index finger for 200 ms. Tactile target stimuli were infrequent and had a gap of 4 ms in the continuous contact after a duration of 98 ms. Tactile stimuli were delivered after 300 ms from the beginning of each trial. From the stimulus onset, participants had 1200 ms to respond. The inter-trial interval (ITI) before the start of the next trial was randomly set between 0 and 400 ms.

Each participant completed three experimental conditions. In all three conditions, participants were required to attend either to their left or right hand, in alternating blocks, and to respond to all tactile target stimuli at that hand. The three experimental conditions differed with respect to the viewing condition under which participants performed the task: in the 'Full vision' condition visual-spatial information about the environment as well as the sight of the participants' hands, and their forearms, were available; in the 'Covered hands' condition only ambient visual-spatial information was available while the participants' hands, as well as their forearms, were covered by a wooden shield which also prevented the view of the space between the hands (Fig. 5.1); and in the 'Blindfolded' condition participants were blindfolded, and therefore neither ambient visual-spatial information nor vision of the hands and arms was available.

Experimental setup

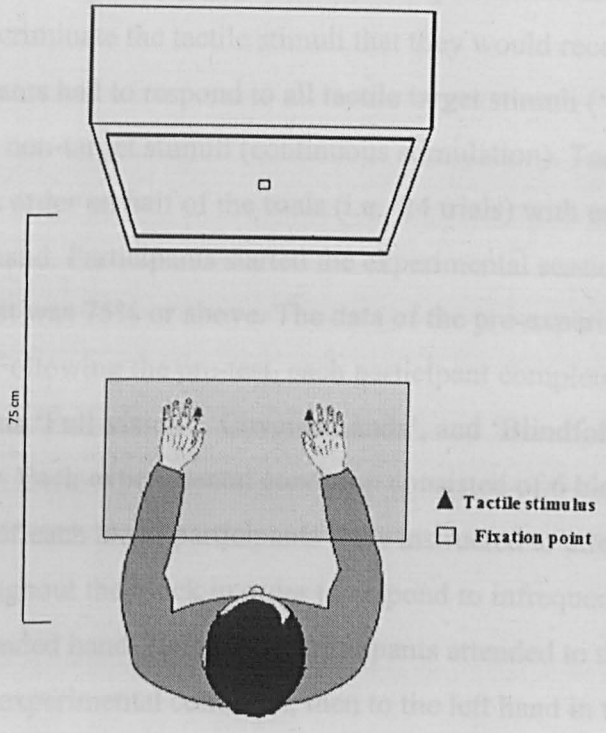


Figure 5.1 Schematic representation of the experimental setup showing the two possible sites of tactile stimulation. In the 'Covered hands' condition, the participants' hands were covered by a wooden shield. This is shown schematically in the figure; the hands are visible in the figure to illustrate their position in all experimental conditions.

In the 'Full vision' and 'Covered hands' conditions, participants were instructed to keep their gaze on a small white fixation square (0.64 cm^2) drawn on a panel at about the participants' eyes level, positioned at a distance of 75 cm from their body. In the 'Blindfolded' condition participants were instructed to keep their eyes open under the blindfold throughout the experiment, and to keep their gaze straight ahead. White noise (50 dB, measured from the position of participant's head) was presented from two loudspeakers placed at 110 cm from the participants' head and equidistant to the right and left of the midline, to mask any sounds made by the tactile stimulators. Participants responded to tactile target stimuli by pressing a pedal with either their right or left foot. Half of participants used their right foot and the other half used their left foot; the foot they had to use to give their responses was assigned at the beginning of the experimental session and was kept constant throughout the three experimental

conditions.

At the start of the experimental session, and before an electrodes cap was mounted on their head, participants carried out a pre-experimental block of 48 trials to ensure they could discriminate the tactile stimuli that they would receive during the experiments. Participants had to respond to all tactile target stimuli ('gap' stimulation) while ignoring tactile non-target stimuli (continuous stimulation). Tactile targets were delivered in a random order on half of the trials (i.e., 24 trials) with equal probability to the right and the left hand. Participants started the experimental session only when their accuracy in the pre-test was 75% or above. The data of the pre-experimental blocks was not analyzed further. Following the pre-test, each participant completed the experimental conditions 'Full-vision', 'Covered hands', and 'Blindfolded' in counterbalanced order. Each experimental condition consisted of 6 blocks of 96 trials each. Before the start of each block participants were instructed to attend either to their right or left hand throughout the block in order to respond to infrequent targets ('gap' stimulation) at the attended hand. Half of the participants attended to their right hand in the first block of each experimental condition, then to the left hand in the second block, and so on; the other half of participants attended to their left hand first. Eight valid tactile targets (i.e., tactile target stimuli delivered to the attended hand which required a foot response), and 8 invalid tactile targets (i.e., target stimuli on the unattended hand which had to be ignored) were delivered in each block. Valid and invalid tactile targets were presented with equal probability to the right or left hand. The remaining 80 trials were non-target trials, which were randomly presented with equal probability to the right and left hand, and required no response. The inter-trial interval between successive stimuli was randomly set between 1500 and 1900 ms.

5.2.3 Recording and Data Analysis

Electroencephalogram (EEG) was recorded from the participants' scalp during each of the three experimental conditions. EEG was recorded with Ag-AgCl electrodes from 28 scalp electrodes (midline electrodes: Fz, Fcz, Cz, Pz; electrodes over the right hemisphere: Fp2, F4, F8, Fc2, Fc6, C4, T8, Cp2, Cp6, P4, P8, O2 and the homologous electrode sites over the left hemisphere), using BrainVision recording system (BrainAmp amplifier and BrainVision Recorder software, version 1.02; Brain Products GmBH, Gilching, Germany; http://www.brainproducts.com). The amplifier bandpass was 0.01-100 Hz. Horizontal electrooculogram (HEOG) was recorded bipolarly from

the outer canthi of both eyes. Electrode impedance was kept below 5 kΩ. EEG and EOG were sampled with a 500 Hz digitization rate, and, subsequently, were digitally filtered off-line with a 40 Hz low pass filter. EEG data were analyzed using BrainVision Analyzer software (version 1.05) (Brain Products GmBH, Gilching, Germany). EEG and EOG were sampled with a 500 Hz digitization rate. EEG and EOG were epoched off-line into 700 ms periods, starting 100 ms before and ending 600 ms after the onset of tactile stimuli. ERPs for tactile non-target stimuli were averaged relative to a 100-ms pre-stimulus baseline. Trials with eye blinks (Fp1 or Fp2 exceeding ± 60 μV relative to baseline), horizontal movements (HEOG exceeding ± 30 μV relative to baseline, approximately equal to ±2.5° of visual angle; see Mangun & Hillyard, 1991) or other artifacts (a voltage exceeding ± 60 μV relative to baseline at electrodes F4, F8, Fc2, Fc6, C4, Cp2, Cp6, P4, P8, and at homologous electrode sites over the left hemisphere) measured within 600 ms after stimulus onset, were excluded from analysis. This procedure led to the removal of about one-fourth of all trials in each single-subject average. ERP analysis was restricted to non-target trials (in which participants responded correctly), and trials immediately following a response were excluded from analysis (10% of total trials on average) in order to avoid contamination of averaged ERPs by movement-related artifacts. The total number of trials that entered the analysis for each single-subject average ranged between 120 and 164 per each of the following six trial types: 'Full vision-attended' and '-unattended', 'Covered hands-attended' and '-unattended', and 'Blindfolded-attended' and '-unattended').

To investigate effects of tactile spatial attention on somatosensory ERPs, statistical analyses (repeated measures ANOVAs) were conducted for recording sites over somatosensory areas, as well as over frontal and parietal areas which are thought to be involved in spatial attention control mechanisms (F3, F4, Fc1, Fc2, Fc5, Fc6, C3, C4, Cp1, Cp2, P3 and P4). ERP mean amplitudes were computed within successive measurement windows centred on the latencies of early somatosensory ERP components. Based on earlier reports and on a visual inspection of the grand averages the following time intervals were analyzed: P100 (75-120 ms after stimuli onset) and N140 (135-180 ms after stimuli onset). Mean amplitudes were also computed for the time interval between 200 and 300 ms post-stimulus in order to investigate longer-latency attentional effects.

To investigate effects of tactile spatial attention on ERPs, separate repeated-measures ANOVAs for the time windows specified above, were carried out with the

factors: viewing condition ('Full vision' vs. 'Covered hands' vs. 'Blindfolded'), attention (attended vs. unattended), electrode (see above), site (frontal, including F3, F4, Fc1, Fc2, Fc5, and Fc6 vs. centro-parietal, including C3, C4, Cp1, Cp2, P3 and P4) and hemisphere (contralateral vs. ipsilateral to the stimulated hand). To investigate effects of tactile spatial attention on response speed to tactile target stimuli, a repeated-measures ANOVA was performed on mean reaction times (RTs) to valid tactile targets between the three viewing conditions ('Full vision', 'Covered hands', 'Blindfolded'). Where Mauchly's test indicated violation of sphericity ($p < 0.05$), we verified repeated-measures results with Greenhouse-Geisser adjustments to the degrees of freedom (ε values are provided when appropriate).

5.3 Results

5.3.1 Behavioural data

Participants missed on average less than 1.5 % of tactile target stimuli; and there was no significant difference between the percentages of missed tactile targets between experimental conditions (see table 5.1). The rate of false alarms to non-target stimuli was on average below 2 %. Trials in which the reaction times (RTs) exceeded ±2 standard deviations from the mean RTs were discarded (leading to the removal of 1.8 % of the trials overall).

Participants' response times (RTs) to infrequent valid tactile target stimuli were on average 21 ms faster under 'Full vision' condition (mean = 521.6 ms) compared to 'Covered hands' condition (mean = 542.6 ms); and 35.3 ms faster compared to 'Blindfolded' condition (mean = 557 ms). A significant effect of viewing condition was obtained in a repeated-measures ANOVA comparing mean RTs to tactile targets under the three viewing conditions ($F_{[2, 22]} = 8.27$, $p < 0.0025$; $\varepsilon = 0.761$). Follow-up paired comparisons revealed a reliable difference between 'Full vision' and 'Covered hands' conditions ($t_{[1, 11]} = 2.85$, $p < 0.02$, 2-tailed), and between 'Full vision' and 'Blindfolded' conditions ($t_{[1, 11]} = 3.80$, $p < 0.004$, 2-tailed), confirming that participants were faster at responding to tactile targets when full visual information was provided compared to when participants' hands were hidden from view, or no visual input was available to participants. Although responses were on average 15.6 ms faster in the 'Covered hands' than in the 'Blindfolded' condition, this difference was not reliable ($t_{[1, 11]} = 0.94$, $p = 0.25$, 2-tailed).

Behavioural results (accuracy and mean RTs)

	Full-vision	Covered hands	Blindfolded
Missed responses	1.1%	1.3%	1.4%
Mean RTs	521.6 ms	542.6 ms	557 ms

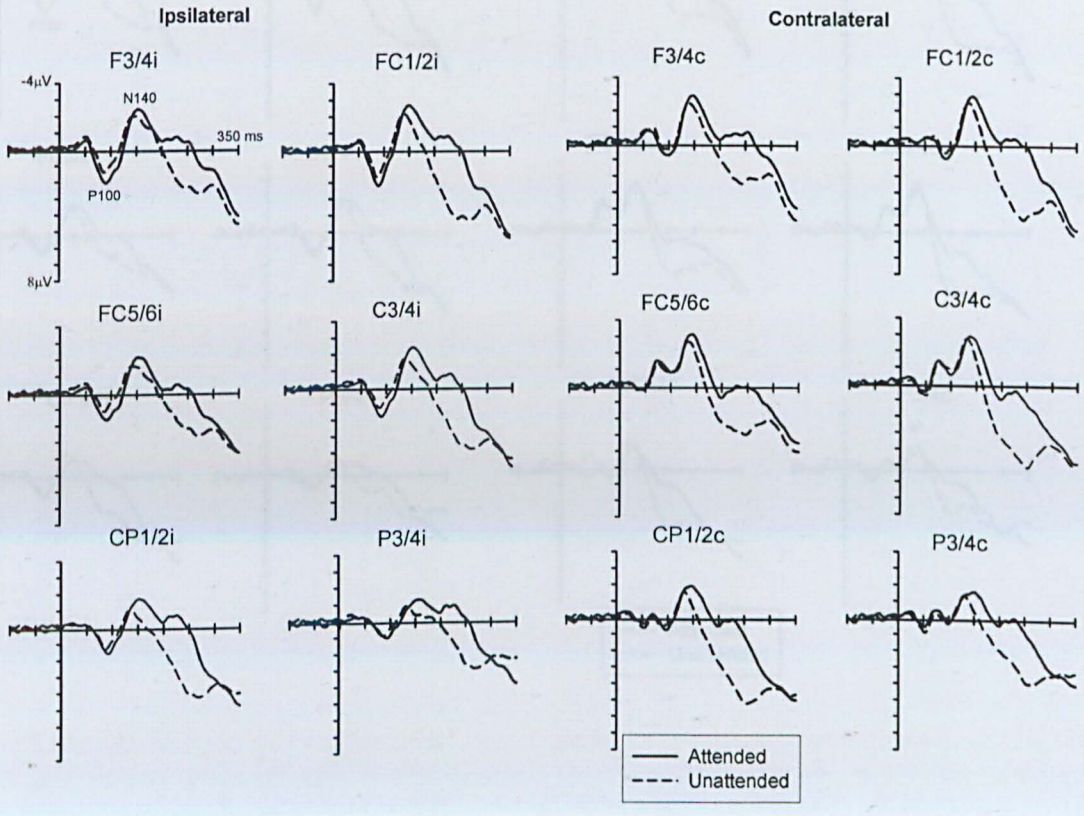
Table 5.1 Percentage of missed responses and mean RTs to tactile target stimuli under the three experimental conditions: 'Full-vision', 'Covered-hands', and 'Blindfolded'

5.3.2 Spatial Attentional Modulations of Somatosensory ERPs

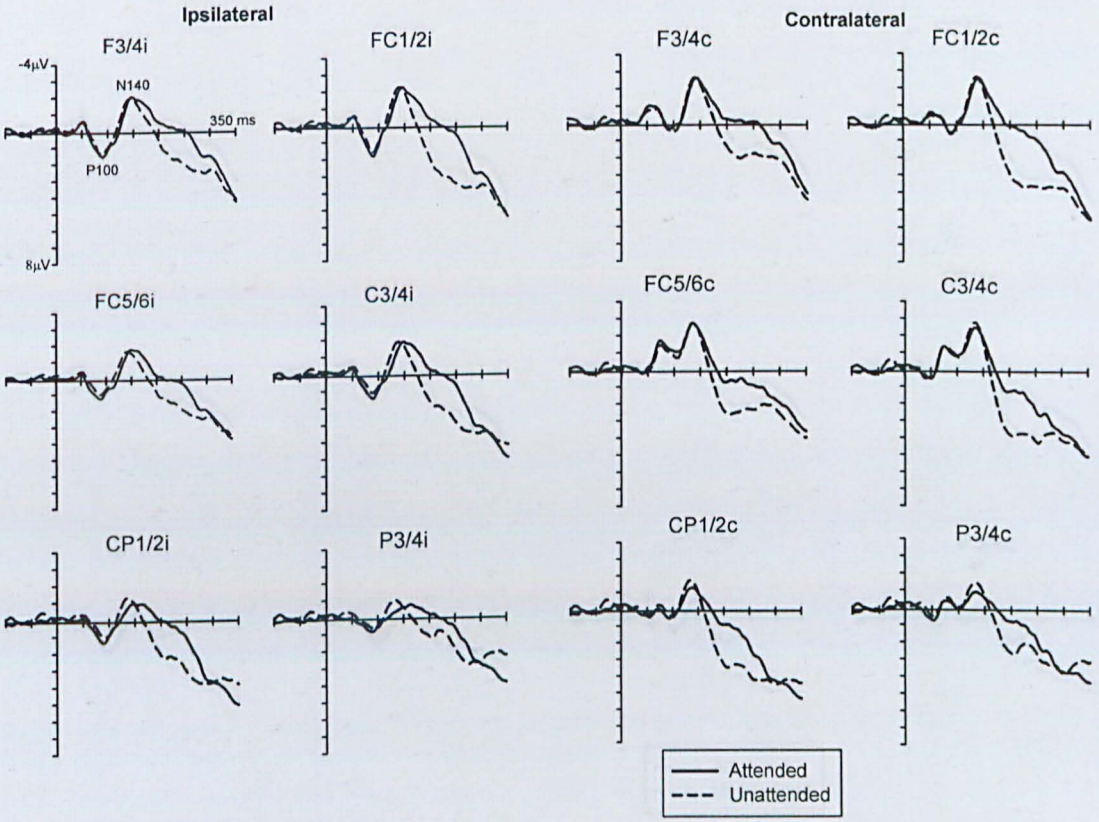
Figure 5.2 shows ERPs elicited by tactile stimuli delivered to the attended (*solid lines*) and to the unattended (*dashed lines*) hand at electrodes contralateral (C) (right side of each panel) and ipsilateral (I) (left side) to the stimulated hand at frontal, central and parietal sites. In panel *a* ERP waveforms are displayed for tactile stimuli delivered in the 'Full-vision' condition; in panel *b* waveforms are shown for the 'Covered-hands' condition; and in panel *c* for the 'Blindfolded' condition. As can be seen from these waveforms, somatosensory ERPs were modulated by tactile-spatial attention, as reflected by greater amplitudes for ERPs in response to tactile stimuli at the attended relative to the unattended hand. However, spatial attentional modulations appear to be present at different time intervals in the three viewing conditions. In particular, while a sustained negativity was elicited at late time intervals (i.e., beyond 200 ms post-stimulus) by attended-hand compared to unattended-hand stimuli in all three viewing conditions, earlier somatosensory components appear to be modulated by attention in the 'Full vision' condition but not in the other two conditions; although in the 'Covered hands' condition, attentional modulations at frontal, but not at parietal, sites may appear to occur somewhat earlier than 200 ms post-stimulus. These differences in the time course of attentional ERP modulations in the three viewing conditions are further illustrated in Figure 5.3. These waveforms were obtained by subtracting ERPs in response to tactile stimuli presented at unattended locations from ERPs elicited by tactile stimuli at attended locations, in each of the three viewing conditions. Difference waveforms are shown for the 'Full vision' (*black solid lines*), the 'Covered hands' (*black dashed lines*), and the 'Blindfolded' (*grey solid lines*) conditions at electrodes contralateral (C) (right side of each panel) and ipsilateral (I) (left side) to the stimulated hand at frontal, central and parietal sites. From these difference waveforms, it can be seen that attentional modulations of somatosensory ERPs occurred earlier and were

enhanced in the 'Full vision' condition compared to the other two viewing conditions, (i.e., 'Covered hands' and 'Blindfolded').

Full-vision' (*a*)



'Covered hands' (*b*)



'Blindfolded' (*c*)

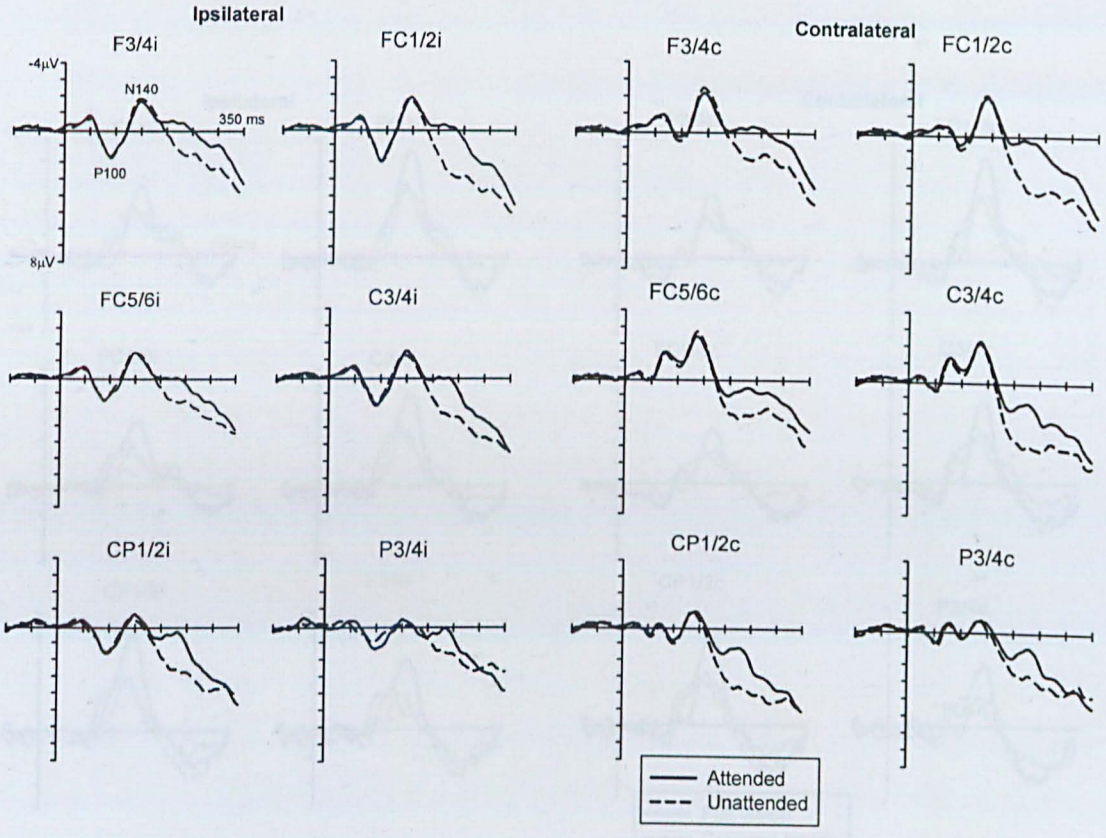


Figure 5.2 Grand-averaged somatosensory ERP waveforms elicited in the experimental conditions 'Full vision' (*a*), 'Covered hands' (*b*), and 'Blindfolded' (*c*) in the 350-ms interval following stimulus onset by tactile non-target stimuli at attended (*solid lines*) and unattended (*dashed lines)* locations. Somatosensory ERPs are shown for electrodes contralateral (right side of each panel) and ipsilateral (left side) to the site of tactile stimulation.

Attentional effects

Difference waveforms:

'Full vision', 'Covered hands', and 'Blindfolded'

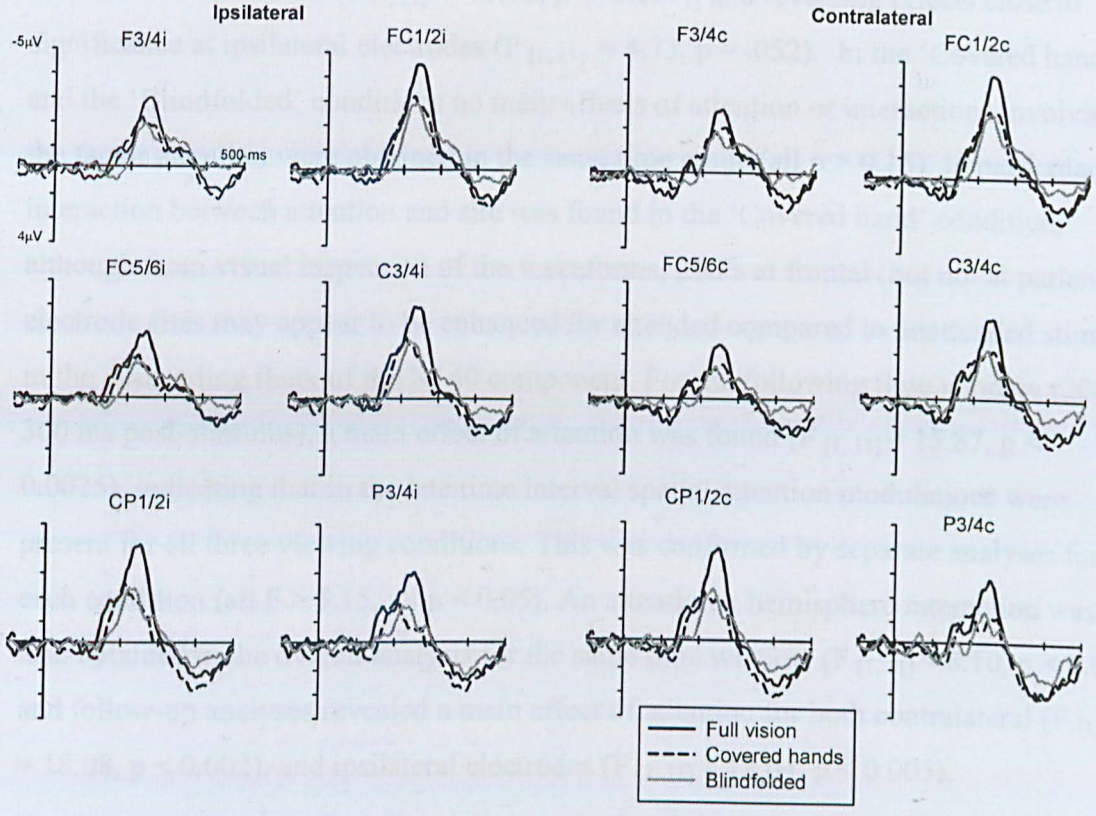


Figure 5.3 Difference ERP waveforms obtained by subtracting ERPs in response to tactile non-target stimuli at attended and unattended locations during the 500-ms interval following stimulus onset, in the experimental conditions 'Full vision' (*black solid lines*), 'Covered hands' (*black dashed lines*), and 'Blindfolded' (*grey solid lines*).

These observations were substantiated by statistical analyses. In the P100 time range (75-120 ms post-stimulus) an attention x viewing condition x hemisphere interaction was present ($F_{[2, 22]} = 4.71$, $p < 0.025$; $\varepsilon = 0.691$). Follow-up analyses, separate for each viewing condition, revealed a significant attention x hemisphere interaction for the 'Full vision' condition ($F_{[1, 11]} = 29.26$, $p < 0.002$), indicating that attention effects were present at ipsilateral ($F_{[1, 11]} = 6.13$, $p < 0.035$) but not at contralateral electrodes ($p = 0.29$). No main effects of attention or interactions involving the factor attention were obtained in the analyses carried out for the 'Covered hands' and the 'Blindfolded' conditions (all $p > 0.13$). In the time window of the subsequent N140 component (135-180 ms post-stimulus) a viewing condition x attention

interaction was obtained ($F_{[2, 22]} = 4.92$, $p < 0.025$; $\varepsilon = 0.704$). Follow-up analyses for each viewing condition showed a main effect of attention ($F_{[1, 11]} = 8.02$, $p < 0.02$) and an attention x hemisphere interaction ($F_{[1, 11]} = 5.89$; $p < 0.035$) in the 'Full vision' condition, with post-hoc analyses confirming the presence of attentional modulations at contralateral electrodes ($F_{[1, 11]} = 11.73$, $p < 0.007$), and revealing effects close to significance at ipsilateral electrodes ($F_{[1, 11]} = 4.73$, $p = .052$). In the 'Covered hands' and the 'Blindfolded' conditions no main effects of attention or interactions involving the factor attention were obtained in the same time range (all $p > 0.15$). In particular, no interaction between attention and site was found in the 'Covered hand' condition, although from visual inspection of the waveforms, ERPs at frontal (but not at pariental) electrode sites may appear to be enhanced for attended compared to unattended stimuli in the descending flank of the N140 component. For the following time window (200-300 ms post-stimulus), a main effect of attention was found ($F_{[1, 11]} = 15.87$, $p < 0.0025$), indicating that in the late time interval spatial attention modulations were present for all three viewing conditions. This was confirmed by separate analyses for each condition (all $F > 5.15$, all $p < 0.05$). An attention x hemisphere interaction was also obtained in the overall analysis for the same time window ($F_{[1, 11]} = 8.10$, $p < 0.02$) and follow-up analyses revealed a main effect of attention for both contralateral ($F_{[1, 11]} = 18.08$, $p < 0.002$), and ipsilateral electrodes ($F_{[1, 11]} = 13.64$, $p < 0.005$).

5.4 Discussion

The aim of the present ERP study was to investigate whether vision modulates mechanisms underlying sustained covert spatial attention to tactile stimuli. In particular, we aimed to clarify whether different levels of visual input (that is, ambient visual-spatial information and vision of the hands) would modulate neural mechanisms of spatial attentional selection at different stages of somatosensory processing. For this purpose, participants performed a tactile attention task under three viewing conditions: full vision, with hands covered from view, and blindfolded. The task required observers to attend to one of the hands throughout a block while maintaining central fixation, in order to detect all tactile target stimuli among non-target stimuli at the currently attended hand.

We found that when participants' hands were visible, attentional ERP modulations, that is, enhanced amplitudes for attended compared to unattended trials,

occurred earlier compared to when no visual input was given (i.e., participants were blindfolded); and, crucially, also compared to when participants' hands were hidden from view and only ambient visual-spatial information was provided. In particular, when full visual information was available, attentional modulations of somatosensory ERPs were found in the time range of the P100 component and of the subsequent N140 component, followed by a sustained negativity for tactile stimuli delivered at attended compared to unattended locations. By contrast, in the other two viewing conditions attentional effects only emerged at later time intervals, about 200 ms after the onset of tactile stimuli, with a sustained negativity for attended compared to unattended stimuli. In addition, the behavioural results were in line with these ERP findings, showing shorter response latencies to tactile target stimuli at the attended hand under full vision condition compared to conditions when the hands were not visible, or participants were blindfolded.

Taken together, the results from the present study show that vision of the body can influence the mechanisms underlying attentional selection within the somatosensory modality. These results are in line with those of a recent PET study (Macaluso et al., 2000b), which showed that the presence of visual input increased activity related to sustained tactile-spatial attention within the intraparietal sulcus, a brain region involved in spatial representation and attention across modalities. Importantly, in that study participants performed a tactile attention task with their eyes open and closed; therefore, the visual modulations of tactile attention effects found by Macaluso and colleagues could be attributed to either the availability of visual information of the environment (which may provide a spatial frame of reference also for modalities other than vision; van Beers et al., 1999; Warren, 1970) or to the sight of the hands in particular, or both. The present study shows for the first time that seeing one's own body (i.e., the hands) while covertly attending to it may be what facilitates sustained attentional processes within the somatosensory modality.

Furthermore, our findings demonstrate that visual information about the hands affects sustained tactile-spatial attention at early stages of processing, as early somatosensory ERP components (namely, the P100 and the N140) were found to be modulated by attention under full visual input. These particular somatosensory components have been shown to originate in secondary somatosensory areas (SII) (Frot & Mauguière, 1999; Hari et al., 1984). This is in contrast to Macaluso et al.'s (2000b) study, where visual modulations of tactile attention effects were only observed in

multimodal intraparietal regions but not in early somatosensory areas such as SI and SII. One important difference that might have contributed to the different results in the two studies is whether tactile stimulation was unilateral or bilateral. In our study participants received tactile stimuli on one hand at a time and had to discriminate their physical properties, which has been shown to take place in primary and secondary somatosensory cortices (Fitzgerald, Lane, Thakur, & Hsiao, 2006; Krupa, Wiest, Shuler, Laubach, & Nicolelis, 2004; Murray & Mishkin, 1984). By contrast, in the study by Macaluso and colleagues' tactile stimulation was always bilateral and tactile targets at the attended hand had to be reported. This task requires perceptual inhibition of stimuli concurrently presented at the unattended location, which is likely to involve higher-order areas, such as the posterior parietal cortex, for the resolution of interference and efficient spatial attentional processing (Geng & Behrmann, 2006; Nassauer & Halperin, 2003; Nee & Jodimes, 2007; Nee, Wager, & Jonides, 2007).

While few formal investigations have been concerned with the effects of visual information about the body on tactile spatial localisation, an ever-growing number of studies have shown that *overt* vision of a body site improves tactile acuity at that particular site in healthy and brain-damaged subjects (e.g., Kennett et al., 2001b; Press et al., 2004; Serino et al., 2007), and enhances early somatosensory ERP components (Taylor-Clarke et al., 2002). This effect has been termed visual enhancement of touch (VET), and it has been suggested to result from descending signals from multisensory areas that may 'pre-activate' the primary somatosensory cortex during vision of the body (Fiorio & Haggard, 2005; Kennett et al., 2001b). In our study a main effect of viewing condition (i.e., irrespective of attention) was not obtained, suggesting that our findings cannot be explained by a mechanism such as VET, perhaps because VET requires direct, not peripheral, vision (e.g., in order to identify the body as one's own body); although it is possible that the easiness of the task may have prevented such an effect (see Press et al., 2004).

Unlike VET, that has been argued not to result from general attentional enhancement (see Fiorio & Haggard, 2005; Kennett et al., 2001), our finding that early attentional ERP effects are modulated by vision suggests that interaction between attention and multisensory processing can influence responses in early somatosensory areas. Evidence from previous studies shows that tactile-spatial attention and vision of the body can (independently and jointly) modulate the activity of somatosensory areas. Previous fMRI and PET studies have suggested that attentional modulations within

early somatosensory areas may rely on feedback projections from associative areas of the fronto-parietal network involved in spatial attention processing, such as the dorsolateral prefrontal cortex and the posterior parietal cortex (Macaluso et al., 2000a; 2002a; Roland 1981, 1982; Schaefer, Heinze, & Rotte, 2005; Staines, Graham, Black, & McIlroy, 2002). In addition, single-cell recordings in animals (see Duhamel et al., 1998; Graziano & Gross, 1993) and neuropsychological and fMRI studies in humans (Làdavas et al., 1998; Làdavas, 2002; Macaluso, 2006; Macaluso & Driver, 2005) have suggested that heteromodal brain regions in frontal and parietal cortices may be involved in crossmodal effects between vision and touch. Attentional and crossmodal areas in frontal and parietal cortices (e.g., the dorsolateral prefrontal cortex involved in attentional processing and the intraparietal sulcus, a multimodal region that may also be involved in body representation) have also been shown to be interconnected via feedforward and feedback projections (Lu et al., 1994; Takada et al., 2004; Tomassini et al., 2007) within a network of attentional and multimodal systems (Calvert, Spence, & Stein, 2004). In line with this, visual modulations of touch suggesting interactions with attentional factors have been reported in healthy observers (Forster & Eimer, 2005) and in the neuropsychological literature (Làdavas et al., 2000). For example, in right-brain damaged patients with spatial attention impairment tactile perception has been shown to be modulated by visual stimuli presented near the patients' stimulated hand, specifically under conditions when that hand was visible (Làdavas et al., 2000).

Taken together, the evidence presented above supports the account that crossmodal interactions (i.e., sight of the touched hands) modulate tactile-spatial attention effects within early somatosensory areas via feedback projections from frontal and parietal regions that are involved in the control of spatial attention and multisensory representation of the body. However, the exact neural mechanisms underlying the effect found in our study remain to be clarified. On the one hand, this modulatory effect could result from *independent* influences from higher-order areas involved in attention and multisensory body representation on somatosensory cortex. On the other hand, interactions between multisensory processing and attention might occur within fronto-parietal areas (see above) before these project back to somatosensory areas. Although both these accounts may be plausible in explaining our findings, two aspects of our results may be in favour of the latter account. First, we did not find an effect of viewing condition independent of attention. In addition, there was no reliable three-way interaction between viewing condition, attention and site (frontal vs. parietal). Although

it does not allow us to draw more specific conclusions about the neural circuit underlying the effects found in this study, this is in accordance with the hypothesis of an involvement of both frontal and parietal cortices in the visual modulation of mechanisms of tactile selection.

It is interesting to note that vision of the hands, rather than ambient visual information alone, was found to be the crucial factor in determining attentional modulations at early somatosensory cortical stages in our study. Ambient visual-spatial information might have been expected to affect tactile-spatial processing because it provides observers with information about the external spatial framework within which tactile events occur, over and above that provided by proprioception. It is thought that tactile events, the location of which can be represented in terms of anatomical and external spatial coordinates, are automatically remapped into an external spatial framework, which is dominated by vision (e.g., Kitazawa, 2002; Pavani et al., 2000). Such remapping is established by the visual system during development, as it occurs in sighted and late blind observers, but not in the congenitally blind (Röder, Rösler, & Spence, 2004; Röder, Föcker, Hötting, & Spence, 2008). Moreover, remapping of touch into an external spatial coordinate system is substantially reduced when the hands are placed at locations for which visual information is limited or is not usually available (behind observers' back; Kobor, Furedi, Kovacs, Spence, & Vidnyanszky, 2006). Visual information about the external environment might thus be expected to aid tactile selection by facilitating remapping of tactile locations into external coordinates. However, in our study facilitation occurred only when visual information included the sight of the hands, and the space around them. Our findings suggest that visual-spatial information per se may not be what drives the dominance of the tactile external coordinate system over a purely anatomical one, but that this dominance is strongly tied to the sight of the hands within it.

Finally, it should be noted that in the 'Covered hand' condition, visual information concerning the position of the hands (e.g., in relation to each other) was not available to the participants, as the space around the hands was also hidden from view. However, visual information about the location of the hands with respect to the body (e.g., hands in front vs. behind the back) and to the external environment was preserved in this experimental condition. We propose that the sight of the body (i.e., the hands) facilitates spatial attentional selection by providing spatial information about the body (e.g., the specific location of body parts) and the space immediately around it. Further

investigations are needed in order to tease apart the specific contribution of (i) sight of the hands and (ii) accurate hand localization, in tactile-attentional modulations.

In conclusion, this study shows that mechanisms of sustained covert spatial attention within the somatosensory modality may operate in a multimodal fashion. In particular, our results demonstrate that attentional effects can occur at earlier stages of somatosensory cortical processing when visual information about the hands and peri-hand space is available. Future investigations with more advanced neuroimaging techniques such as diffusion tensor imaging (DTI), in combination with functional magnetic resonance imaging (fMRI), could help clarify the specific neural pathway involved in interactions between spatial attention and sight of the body as those observed in the present study.

Chapter 6

Visual and proprioceptive modulation of tactile extinction: behavioural and electrophysiological evidence

Crossing the hands over the mid-sagittal plane of the body, so that the left hand is placed in the right-hand-side of egocentric space, reduces left tactile extinction to double simultaneous stimulation in right-brain-damaged patients. We investigated whether the position of the left hand (crossed vs. uncrossed), and the vision of that hand, affect the processing speed of tactile stimuli. In addition, we sought for the possible brain mechanisms of such effects. Four right-brain-damaged patients with left visuo-spatial neglect and/or left-sided tactile extinction to double simultaneous stimulation (three patients) or hypoaesthesia (one patient), and eight neurologically unimpaired participants received single taps to their left index finger, and were asked to report by a vocal response each detected tactile stimulus. The participants' left hand was either in an 'uncrossed' anatomical position, in the left-hand-side of space, contralateral to the side of the patients' lesion (contralesional), or 'crossed' over the midline, in the right-hand-side of space, ipsilateral to the side of the hemispheric lesion (ipsilesional). Vision of the left hand was either available or prevented. Somatosensory event-related brain potentials (ERPs) were recorded from one patient and two control participants, in response to the stimulation of the left hand in both the 'uncrossed' and 'crossed' positions. In the patients, crossing of the left hand resulted in a decrease in response times (RTs) to tactile stimuli, particularly when the hand was visible. By contrast, in the unimpaired participants crossing the left hand increased RTs. The ERP results were in line with the behavioural findings. In the patient, the somatosensory P70, N140, and N250 components were enhanced for the 'crossed' position. By contrast, in the control participants the early somatosensory ERP components were not modulated by hand position. In sum, in right-brain-damaged patients with left spatial neglect, moving the left hand towards the right-hand-side of space improved somatosensory processing, as indexed by RTs. This spatial effect may rely on a

modulation of stimulus processing taking place as early as in primary somatosensory cortex (SI).

6.1 Introduction

Awareness of sensory stimuli (e.g., tactile, visual) can be impaired by brain damage. Unilateral hemispheric lesions involving the somatosensory and visual systems may bring about contralesional deficits (hemianaesthesia, hemianopia) (Adams, Victor, & Ropper, 2005). Somatosensory and visual half-field deficits are more frequent after right hemispheric than after left hemispheric lesions (Sterzi, Bottini, Celani, Righetti, Lamassa et al., 1993). This hemispheric asymmetry cannot be accounted for in terms of primary sensory deficits, suggesting instead a higher-order impairment related to the right hemispheric damage and to deficits of spatial representation and attention (Vallar, 1998). Moreover, there is electrophysiological (Eimer, Maravita, Van Velzen, Husain, & Driver, 2002; Vallar, Bottini, Sterzi, Passerini, & Rusconi, 1991; Vallar, Sandroni, Rusconi, & Barbieri, 1991), anatomical (Driver & Vuillemier, 2001), as well as fMRI (Kobayashi, Takeda, Kaminaga, Shimizu, & Iwata, 2005) evidence that primary sensory pathways may be intact in these patients.

A more specific indication of a spatial, rather than purely sensory, component of the somatosensory deficits of right-brain-damaged patients has been provided by the finding that irrigating the left external ear canal with cold water, or the right canal with warm water (caloric vestibular stimulation) temporarily ameliorates somatosensory deficits and extinction to double simultaneous stimulation in right-brain-damaged patients (Bottini et al., 2005; Vallar, Bottini, Rusconi, Sterzi, 1993; Vallar, Sterzi, Bottini, Cappa, & Rusconi, 1990). As caloric stimulation improves many higher-order (spatial) aspects of the neglect syndrome (Vallar, Guariglia, & Rusconi, 1997), this result suggests that somatosensory deficits may have non-sensory components, related to the impairment of spatial representations of corporeal space, contributing to perceptual awareness of tactile stimuli (Gallace & Spence, 2007; Vallar, 2007).

A converging source of evidence comes from studies that have manipulated the posture of the participants' hands, with the aim of disentangling the relative contribution of the somatotopic and higher-order spatial reference frames in modulating the somatosensory deficits exhibited by right-brain-damaged patients (Aglioti, Smania & Peru, 1999; Moscovitch & Behrmann, 1994; Smania & Aglioti, 1995). Brain-damaged

patients with contralesional spatial neglect or extinction fail to report somatosensory stimuli delivered to the contralesional side of either wrist when both sides of the wrist are simultaneously stimulated, regardless of whether the patients' hands are positioned palm up or palm down (Moscovitch & Behrmann, 1994). That is, irrespective of hand posture, patients extinguish the left-most stimulus with reference to the spatial, not to the sensory (somatotopic), coordinates frames. Similarly, the ability of right-brain-damaged patients to detect left-sided stimuli (both single and associated with a simultaneous right-sided touch) improves when their hands are crossed over the midline, so that the left hand is placed in the right-hand side of space (ipsilesional) and vice versa (Aglioti et al., 1999; Moro, Zampini, & Aglioti, 2004; Smania & Aglioti, 1995). These results suggest that higher-order, spatial impairments contribute to the somatosensory deficits of right-brain-damaged patients with left tactile extinction or neglect. However, as in the abovementioned studies participants were blindfolded, the contribution of the vision of the stimulated hand to these somatosensory disorders remains unexplored. Spatial frames of reference are dominated by vision (Eimer, 2004; Röder et al., 2004; Shore, Spry, & Spence, 2002), which is the most accurate sensory modality for spatial perception in humans (Bolognini & Maravita, 2007; Warren, 1970; Warren & Pick, 1970), at least in the azimuthal (left-right) direction (van Beers et al., 1999). Furthermore, crossmodal links between vision and touch (Botvinick & Cohen, 1998; Maravita, Spence, & Driver, 2003; Serino et al., 2007; Taylor-Clarke et al., 2002; Tipper et al., 1998, 2001), and between vision and proprioception (Botvinick & Cohen, 1998; Graziano, 1999; Lloyd, Shore, Spence, & Calvert, 2003; Maravita et al., 2003; van Beers, Sittig, & Denier van der Gon, 1996, 1999) have been extensively shown, including the integration between visual and proprioceptive cues in localizing limb position and tactile sensations (Botvinick & Cohen, 1998; Graziano, 1999; van Beers et al., 1999). Accordingly, the prediction can be made that non-informative vision of the stimulated hand may modulate spatial effects on tactile detection by right-brain-damaged patients.

In this study, we first tested whether, in right-brain-damaged patients with left spatial neglect and left tactile extinction, latencies to unilateral touches delivered to the left hand are affected by its spatial position (namely, in an 'uncrossed' anatomical position, in the left hand-side of space, or in a 'crossed' position, in the right-hand side of space, with reference to the mid-sagittal plane of the body), and by the vision of the hand. Should tactile stimuli be perceived and localized first according to egocentric

coordinates (namely, at the location where the stimulated body part lies), and then in somatotopic coordinate frames ("on the skin") (Kitazawa, 2002), then somatosensory stimuli delivered to the left hand should undergo better processing when that hand is positioned in the right (non-neglected), rather than in the left, side of space. Moreover, the patients' detection of somatosensory stimuli delivered to the left hand would improve even further when that hand is visible under 'crossed' position.

Finally, the present study investigated the neural correlates of the 'crossed-hand' effect on somatosensory perception in right-brain-damaged patients, an issue that has not been hitherto addressed. Particularly, by recording event-related potentials (ERPs), we addressed the question of which stages of somatosensory processing are modulated by the spatial position of the left hand. To this aim, in one patient and in two age-matched neurologically unimpaired control participants, we compared ERPs elicited by tactile stimuli delivered to the left hand in 'uncrossed' anatomical position (i.e., in the left side of space), or 'crossed' over the midline in the right side of space.

6.2 Simple reaction time (SRT)

6.2.1 Methods

6.2.1.1 Participants

Four right-brain-damaged (RBD) patients with left-tactile extinction or neglect (mean age: 62 years, see Table 6.1), and eight age-matched, neurologically unimpaired control participants (mean age: 64.5 years, range: 31-87; mean years of education: 10.25, range 3-17) entered this study. Three patients were recruited from the Neuropsychological Laboratory of the IRCCS Istituto Auxologico Italiano, Milano, Italy, and one from the Rehabilitation Unit, Ospedale "C. Poma", Bozzolo, Mantova, Italy. All patients, and the control participants, gave their informed consent to the study. The patients' demographic, neurological, and neuropsychological characteristics are summarized in Table 6.1. The lesion of patient #1, who participated in the ERP experiment, is shown in Figure 6.1. Motor, somatosensory and visual field deficit were assessed by a standard neurological exam (Bisiach & Faglioni, 1974).

Table 6.1

P.	Sex/Age	Schooling (years)	Aetiology/ Lesion site	Duration of disease (months)	Neurological deficits M	SS	VF	Line bisection (%)	Cancellation tests Line (%)	Letter (%)
1	M/77	illitterate	I/BG/ pvwm	14	1	2	2	+14.2	0	17
2	M/36	9	#/H/BG/FTP	12	1	0	0	+11.2	63	6
3	M/76	17	I/FTP/ pvwm	11	1	e	e	+11.6	36	100
4	M/69	7	I/FTP	1	3	3	3	n/a	n/a	79

Table 6.1 Demographic, neurological and neuropsychological characteristics of four right-brain-damaged right-handed patients (P.). I/H: infarction, haemorrhage; #: surgical evacuation of an intracerebral hemathoma; clamp of the middle cerebral artery. F, T, P: frontal, temporal, parietal cortico-subcortical damage; BG: basal ganglia; pvwm: periventricular white matter. Neurological impairment (M: motor; SS: somatosensory; VF: visual field): 1 (mild), 2 (moderate), 3 (severe) impairment; 0 (no deficit); e: extinction to double simultaneous stimulation. Cancellation tests: percent left-sided omissions; n/a: not available. Neurological and neuropshychological data reported here were acquired three months (patient #1 and #2), six months (patient #3), and two weeks (patient #4) following stroke onset in each patient.

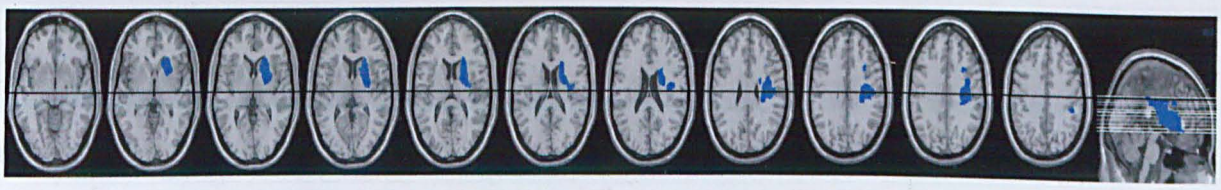


Figure 6.1 Patient #1. A CT-Scan performed two months after stroke onset showed an hypodense right-hemispheric lesion involving the head of the caudate nucleus, the putamen, and the paraventricular fronto-parietal white matter; the frontal horn of the right-sided ventricle was compressed.

6.2.1.2 Neuropsychological assessment

Unilateral visuo-spatial neglect was assessed using three cancellation tests:

1) Line cancellation (Albert, 1973). The scores were the numbers of cancelled line targets in the left- and right-hand sides of the sheet (range 0-21). Marks such as lines, crosses, or dots systematically placed in the close proximity of each line were considered as correct cancellations. Neurologically unimpaired participants have a flawless performance on this task.

2) Letter cancellation (Diller, Ben-Yishay, Gerstman, Goodkin, Gordon, &

Weinberg, 1974). The patients' task was to cross out all of 104 H letters (53 in the left-hand side, and 51 in the right-hand-side of the sheet), printed on an A3 sheet together with other letter distracters. In neurologically unimpaired subjects the maximum difference between the omission errors on the two sides of the sheet was two (Vallar, Rusconi, Fontana, & Musicco, 1994).

3) Line bisection. The patients' task was to mark with a pencil the mid-point of six horizontal black lines (two 10 cm, two 15 cm, and two 25 cm in length, all 2 mm in width), presented in a random fixed order. Each line was printed in the centre of an A4 sheet, aligned with the mid-sagittal plane of the participant's body. The length of the left-hand side of the line (i.e., from the left end of the line to the subject's mark) was measured to the nearest mm. That measurement was converted to a standardized score (percent deviation): measured left half minus objective half/objective half x 100 (Rode, Michel, Rossetti, Boisson, & Vallar, 2006). This transformation yields positive numbers for marks placed to the right of the physical centre, and negative numbers for marks placed to the left of it. The mean percent deviation score of ten neurologically unimpaired participants (mean age: 72.2, SD: 5.27, range: 67-82; mean years of schooling: 9.2, SD: 6.21, range 3-18) was +0.54% (SD: 0.02, range -2 % +4.8%).

6.2.1.3 Assessment of tactile perception

The patients' ability to report single and double somatosensory stimuli was assessed by a computer-driven test. This consisted of 60 stimuli, with 20 tactile stimuli being delivered to the left hand, 20 to the right hand, and 20 bilaterally, in a fixed random order. Tactile stimuli were delivered using 12V solenoids, driving a metal rod with a blunt conical tip that contacted the top segment of the index finger for 200 ms. Participants fixated a cross drawn on a paper sheet placed on the table where they rested their left arm; the fixation cross was aligned with the mid-sagittal plane of the participants' body, at a distance of about 40 cm. Participants received instructions to report verbally the occurrence and side of each delivered tactile stimulus (i.e., left-sided, right-sided, or bilateral). Patients were considered to show left-sided extinction when over 80% of unilateral left-sided tactile stimuli were reported correctly, and the left-sided stimulus of a bilateral stimulation was not reported in more than 30% of the trials. The patients' performance is shown in Table 6.2. Three out of four patients showed left tactile extinction, while patient #4 missed 85% of the unilateral left-sided stimuli. The

errors on bilateral trials always consisted of left-sided omissions. All control participants performed at ceiling with both unilateral and bilateral stimuli.

Table 6.2

Stimulation:	Right-sided	Left-sided	Bilateral
Patient 1	90%	95%	10%
Patient 2	100%	85%	0%
Patient 3	100%	85%	0%
Patient 4	85%	15%	0%
Control group (average)	100%	100%	100%

Table 6.2 Percent correct detections of computerized tactile stimuli.

6.2.1.3 Apparatus and Procedure

A speeded tactile detection task was administered, consisting of eight experimental blocks, each including 40 trials. Tactile stimuli were delivered to the participants' left index finger in 30 trials per block. The remaining 10 were 'catch trials' in which no stimulation was given. Tactile stimuli were delivered using a 12V solenoid (see above), and consisted of single taps lasting for 200 ms. In alternating blocks, the participants' left hand was either in anatomical ('uncrossed') position (i.e., in the patients' contralesional left hand-side of space), or 'crossed' over the midline (i.e., in the patients' ipsilesional right hand-side of space), with the vision of the left hand being either available or prevented. The distance of the participants' left hand from the body was about 35 cm. The right arm was always held along the body and hidden from view. Participants performed four experimental conditions: 'crossed-seen', 'crossed-unseen', 'uncrossed-seen', and 'uncrossed-unseen'. Two blocks were performed for each condition in an ABCDDCBA order ('crossed-seen', 'crossed-unseen', 'uncrossed-seen', 'uncrossed-unseen', then the reverse) for half of the participants, and the reversed order for the other half of the participants. A wooden box (70 cm wide x 35 cm deep x 10 cm tall) covered the participants' left hand (and forearm) in the two 'unseen' conditions. A central, squared aperture (side 15 cm) in the box allowed participants to see the fixation

cross. Visual information about the position of the hand (crossed or uncrossed) was prevented by the box during the 'unseen' conditions; therefore in these conditions participants could rely only on proprioceptive cues for hand localization (see Fig. 6.2). Participants were instructed to fixate the cross throughout each block, and make a vocal response ('one') as quickly as possible whenever a tactile stimulus was detected. Vocal reaction times (RTs) were recorded by a voice key. Participants were allowed 2000 ms to respond after the stimulus presentation. Then the experimenter entered the participants' response ('1' when participants said 'one', and '0' for no response), and pressed a key on the computer keyboard for the next trial after checking for fixation, and ensuring that the participant was ready to proceed. Patient #4, because of his low accuracy in the detection task, completed two sessions of eight blocks each (i.e., 16 blocks in total), to provide enough trials for RTs analysis.

Experimental setup

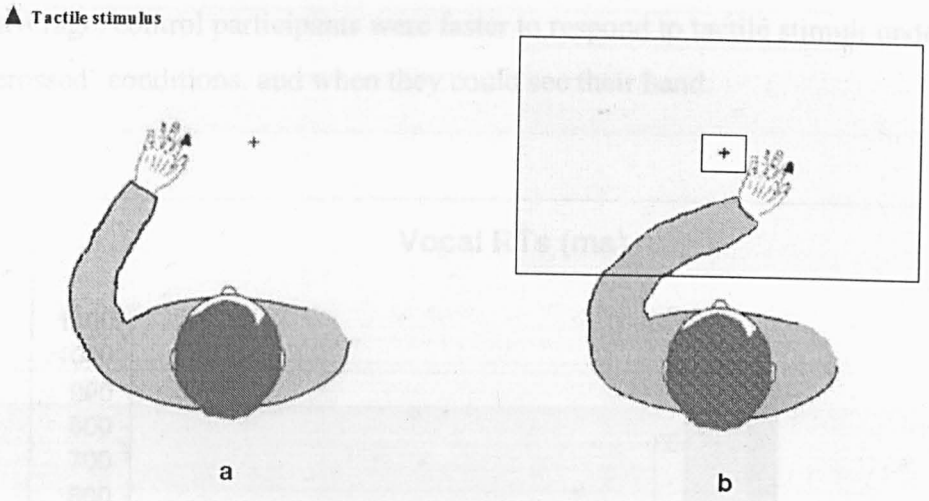


Figure 6.2. Schematic representation of the experimental setup showing the position of the left hand in space, i.e., in the left hemispace ('uncrossed' position, a) and in the right hemispace ('crossed' position, b). The right arm was held along the body and hidden from view, as shown in the bird's-eye view image. The tactile stimuli were applied to the tip of the participants' index finger. In b, a schematic representation of the box used to cover the participants' left hand and forearm is shown. In the figure, the arm is visible under the box to illustrate the 'crossed' position.

6.2.2 Results

Figure 6.3 shows mean vocal RTs to left-sided tactile stimuli and standard errors for each of the patients and for the controls' group, for the four experimental conditions (i.e., 'crossed-seen', 'crossed-unseen', 'uncrossed-seen', and 'uncrossed-unseen'). Patients #1, #2, and #3 and control participants missed on average less than 1% of tactile stimuli (range: 0-2.2%). Patient #4 missed 44% of the stimuli in the 'crossed-seen' condition, 46% in the 'crossed-unseen' condition, 65% in the 'uncrossed-seen' condition, and 77% in the 'uncrossed-unseen' condition. The average false alarm rate for all participants (patients and controls) was 1.2% (range: 0.3-2.4%). For each participant, trials in which the RTs exceeded ±3 SD from the participant's average RTs within each condition were discarded. This procedure led to the removal of 2.3% of the

trials overall. As shown in Figure 6.3, all patients were faster at responding to tactile stimuli in the 'crossed' compared to the 'uncrossed' conditions, at least when vision of the hand was available (i.e., 'crossed-seen' trials). Moreover, all patients responded faster in the 'crossed-seen' compared to 'crossed-unseen' trials, while three out of four patients were slower in the 'uncrossed-seen' compared to the 'uncrossed-unseen' trials. On average, control participants were faster to respond to tactile stimuli under 'uncrossed' conditions, and when they could see their hand.

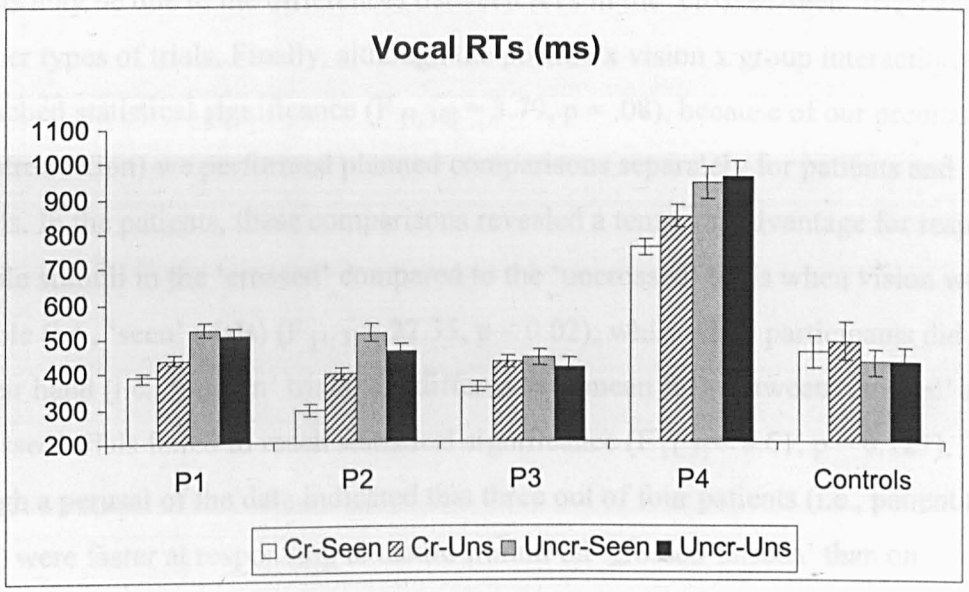


Figure 6.3 Mean vocal RTs to left-sided tactile stimuli and standard errors are shown for each of the patients (P1 to P4) and for the control group in the four experimental conditions (Cr-Seen: 'crossed-seen'; Cr-Uns: 'crossed-unseen'; Uncr-Seen:'uncrossed-seen'; Uncr-Uns:'uncrossed-unseen').

A repeated-measures ANOVA was performed in patients and controls on the mean vocal RTs to tactile stimuli delivered to the left hand, with the main within-subjects factors hand position (crossed vs. uncrossed), and vision (seen vs. unseen), and with 'group' as a between-factor. This analysis revealed a main effect of hand position ($F_{[1, 10]} = 5.56$, $p < .05$), with overall faster RTs to tactile stimuli on 'crossed' (M = 481) than on 'uncrossed' (M = 513 ms) trials overall. Critically, however, while the mean response latencies in the patients' group were shorter for the 'crossed' (M = 489 ms) than for the 'uncrossed' (M = 585 ms) trials, the controls showed the reverse pattern of results (M = 474 ms for 'crossed' vs. 431 ms for 'uncrossed' trials), resulting in a hand position x group interaction ($F_{[1, 10]} = 31.91$, $p < .002$). Post-hoc comparisons confirmed the presence of significant effects of hand position on RTs in both groups ($F_{[1, 3]} =$

16.43, $p < 0.03$ in the patients, and $F_{[1, 7]} = 11.27$, $p < 0.02$ in the controls). In addition, a main effect of vision ($F_{[1, 10]} = 8.17$, $p < 0.02$) was present in the overall analysis indicating that participants were significantly faster at responding to tactile stimuli when their hand was visible (486 vs. 509 ms). A hand position x vision interaction was also found overall ($F_{[1, 10]} = 8.58$, $p < 0.02$), and pairwise comparisons revealed faster mean RTs on 'crossed-seen' trials compared to 'crossed-unseen' trials ($t_{[1, 11]} = -3.03$, $p < 0.02$; for all other comparisons $p > 0.05$). This significant hand position x vision interaction suggests that the main effects of hand position and of vision in the overall analysis may be due to the differences between RTs in the 'crossed-seen' trials and all the other types of trials. Finally, although the posture x vision x group interaction only approached statistical significance ($F_{[1, 10]} = 3.79$, $p = .08$), because of our predictions (see Introduction) we performed planned comparisons separately for patients and controls. In the patients, these comparisons revealed a temporal advantage for responses to tactile stimuli in the 'crossed' compared to the 'uncrossed' trials when vision was available (i.e., 'seen' trials) ($F_{[1, 3]} = 27.35$, $p < 0.02$); while when participants did not see their hand (i.e., 'unseen' trials) the difference in mean RTs between 'crossed' and 'uncrossed' trials failed to reach statistical significance ($F_{[1, 3]} = 4.61$, $p = 0.121$), although a perusal of the data indicated that three out of four patients (i.e., patient #1, #2, #4) were faster at responding to tactile stimuli on 'crossed-unseen' than on 'uncrossed-unseen' trials. In addition, planned comparisons revealed a significant difference in mean response latencies between 'crossed-seen' and 'crossed-unseen' trials, reflecting faster responses for the former ($F_{[1, 3]} = 41.98$, $p < 0.01$); whereas the difference between 'uncrossed-seen' and 'uncrossed-unseen' trials was not significant ($F_{[1, 3]} = 2.21$, $p = 0.23$). In the controls' group, the same comparisons revealed no significant difference in response latencies (all $F < 2.23$, all $p > 0.34$), although RTs were 30 ms faster under 'crossed-seen' compared to 'crossed-unseen' trials.

6.3 Somatosensory Event-Related Potentials (ERPs)

6.3.1 Methods

6.3.1.1 Participants

Somatosensory event-related brain potentials (ERPs) were recorded from patient #1 (see Table 6.1), and from two neurologically unimpaired age-matched male controls

(Control #1, 78 year-old; Control #2, 80 year-old), who did not take part in the simple reaction time (SRT) experiment. All participants gave written informed consent.

6.3.1.2 Apparatus and Procedure

The general experimental set-up and procedures were similar to those of the SRT experiment, with the following differences. First, vision of the hands was available in all trials. Thus, participants performed the task under two experimental conditions, i.e., 'uncrossed' vs. 'crossed' position of the left hand (see section 6.2.1.4), in alternating blocks. Second, in order to increase the number of critical left stimulations for the purpose of statistical analysis, a greater number of trials was given. Patient #1 was tested in two sessions, separated by 8 days. The two control participants completed one single experimental session. Each session consisted of eight blocks with 50 trials per block, including 40 left-sided touches and 10 'catch trials' (absent stimulation).

6.3.1.3 EEG Recording and Data Analysis

EEG was recorded with Ag-AgCl electrodes from 28 scalp electrodes (midline electrodes: Cz, Pz, POz, Oz; electrodes over the right hemisphere: Fp2, F4, F8, C4, T8, TP8, Cp4, P4, P8, PO4, PO8, O2 and the homologous electrode sites over the left hemisphere), using BrainVision recording system (BrainAmp amplifier and BrainVision Recorder software, version 1.02; Brain Products GmBH, Gilching, Germany; http://www.brainproducts.com). The amplifier bandpass was 0.01-100 Hz. Horizontal electrooculogram (HEOG) was recorded bipolarly from the outer canthi of both eyes. Electrode impedance was kept below 5 kΩ. EEG and EOG were sampled with a 500 Hz digitization rate, and, subsequently, were digitally filtered off-line with a 40 Hz low pass filter. EEG data were analyzed using BrainVision Analyzer software (version 1.05) (Brain Products GmBH, Gilching, Germany). EEG and EOG were epoched off-line into 450 ms periods, starting 100 ms before and ending 350 ms after the onset of tactile stimulation. ERPs for tactile stimuli were averaged relative to a 100-ms pre-stimulus baseline. Trials with eye blinks and movement-related artifacts (EEG waveforms exceeding ± 80 μV relative to baseline), measured at any recording sites within 350 ms after stimulus onset, were excluded from analysis. ERP waveforms were averaged relative to a 100 ms pre-stimulus baseline, separately for 'uncrossed' and 'crossed' trials. The total number of trials contributing to the resulting average waveforms (collapsed across the two sessions) for patient #1 was 201 for 'uncrossed' and 189 for

'crossed' trials. For the statistical analysis of the patient's data, each of the two sessions was further subdivided into two sub-sessions for a total of four sub-sessions for each experimental condition ('uncrossed' vs. 'crossed'). The mean number of trials contributing to the average ERPs for each sub-session was 62.75 (range: 54 to 78) (for a similar statistical method see Eimer et al., 2002; Marzi, Girelli, Miniussi, Smania, & Maravita, 2000). For the statistical analysis of the controls' data, each participant's session was subdivided into two sub-sessions, producing a total of four sub-sessions for each of the two left hand positions ('uncrossed' vs. 'crossed') for the two participants. The mean amplitudes of early somatosensory ERP components (P70 and N140) were computed within analysis windows centred on the peak latency of these components as appeared from the practice data. As the N140 component was somewhat delayed in both control participants compared to the N140 component observed in patient #1 (see Fig. 6.4 and 6.5), two distinct time windows were computed for this component centred on the peak of the N140 in the patient (N140p) and on the peak of the N140 in the controls (N140c). In addition, in order to investigate longer-latency effects of hand position on somatosensory ERPs, mean amplitudes were also computed within the analysis window centred on the peak latency of the patient's N250 component (N250p). This component was absent in the ERP waveforms of both control participants, who showed a 'sustained negativity' beyond 220 ms post-stimulus onset. Thus, mean amplitude values were computed for the following post-stimulus latency windows in all participants: 55-90 ms post-stimulus onset (P70), 105-155 ms post-stimulus onset (N140p), 150-195 ms post-stimulus onset (N140c), 235-270 ms post-stimulus onset (N250p), and 220-350 ms post-stimulus onset. Analyses of ERP data were restricted to centro-parietal electrodes contralateral to the side of stimulation where somatosensory ERP components are maximal. Separate repeated-measures ANOVAs were conducted on mean amplitudes for the P70, N140p, N140c, and N250p components, and for the 220-350 ms post-stimulus measurement window, separately for the patient and the controls, with the factors hand position (uncrossed vs. crossed) and electrode site (C4 vs. CP4 vs. P4), with hand position as a between-group factor, where 'group' refers to the sub-sessions obtained for different hand position conditions (see above).

6.3.2 Results

Figure 6.4 displays somatosensory ERPs recorded from patient #1 in response to left tactile stimuli delivered when the left (contralesional) hand was in an 'uncrossed' (anatomical) position (*solid line*), and 'crossed' over the midline (*dashed line*). As can be seen from these waveforms, left tactile stimuli elicited a positive-going deflection peaking at about 70 ms after onset of the stimulus (i.e., somatosensory P70 component) followed by two negative deflections with a latency of about 140 ms (i.e., overlapping with the somatosensory N140 component), and 250 ms (i.e., overlapping with the somatosensory N250 component). These components were maximal at centro-parietal electrode sites (i.e., C4, CP4, and P4). As shown in Figure 6.4, tactile stimuli elicited enhanced P70, N140 and N250 amplitudes when the patient's left hand was placed in the right-hand-side of space ('crossed' trials), compared to when that hand was held in the left-hand-side of space ('uncrossed' trials). Similarly to the somatosensory ERPs recorded from one right-brain-damaged patient in a previous study (Eimer et al., 2002), somatosensory N80 and P100 components that are typically evoked by tactile stimuli in neurologically unimpaired subjects (e.g., Eimer & Forster, 2003a; Michie et al., 1987; Taylor-Clarke et al., 2002) were not apparent in the patient's waveforms. Conversely, these components were present in the ERP waveforms of both control participants, following the P70 component (see Figure 6.5). Importantly, Figure 6.5 suggests that in the control participants the very early somatosensory components were not modulated by the spatial position of the stimulated hand, while the pattern of modulations at later latencies was the reverse of that shown by the patient. That is, in Control #1 (Fig. 6.5a) modulations of the electrophysiological responses following hand position change were present from 200 ms post-stimulus where a sustained negativity was evident for tactile stimuli delivered in the 'uncrossed' compared to the 'crossed' condition; and in Control #2 (Fig. 6.5b) the amplitude of the somatosensory N140 component was somewhat larger for tactile stimuli delivered under 'uncrossed' compared to 'crossed' position, and this modulation was followed by a sustained negativity similar to Control #1.

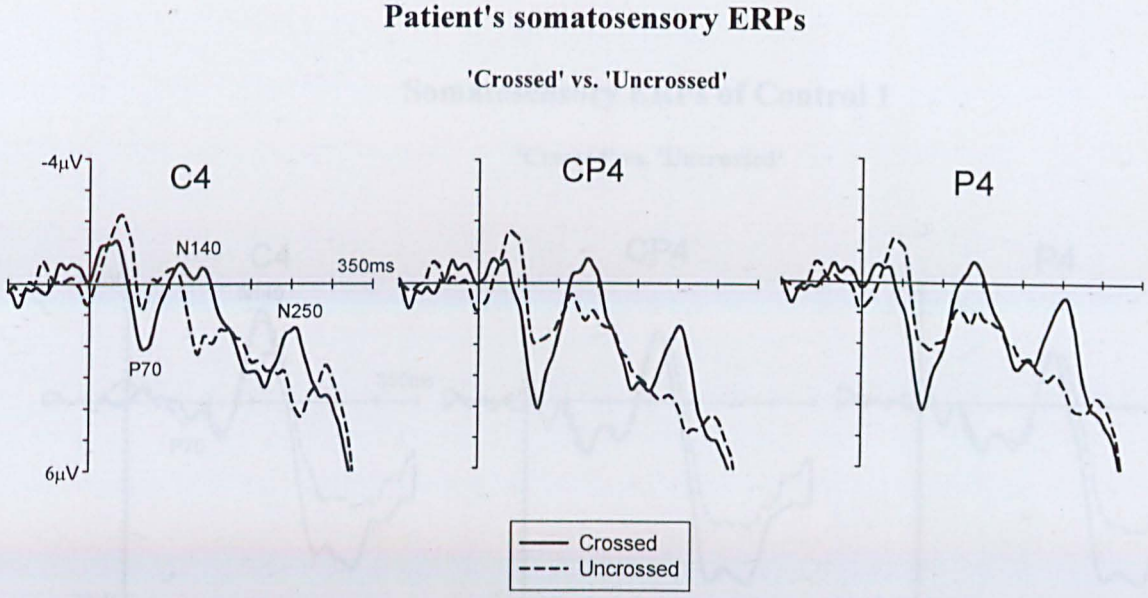
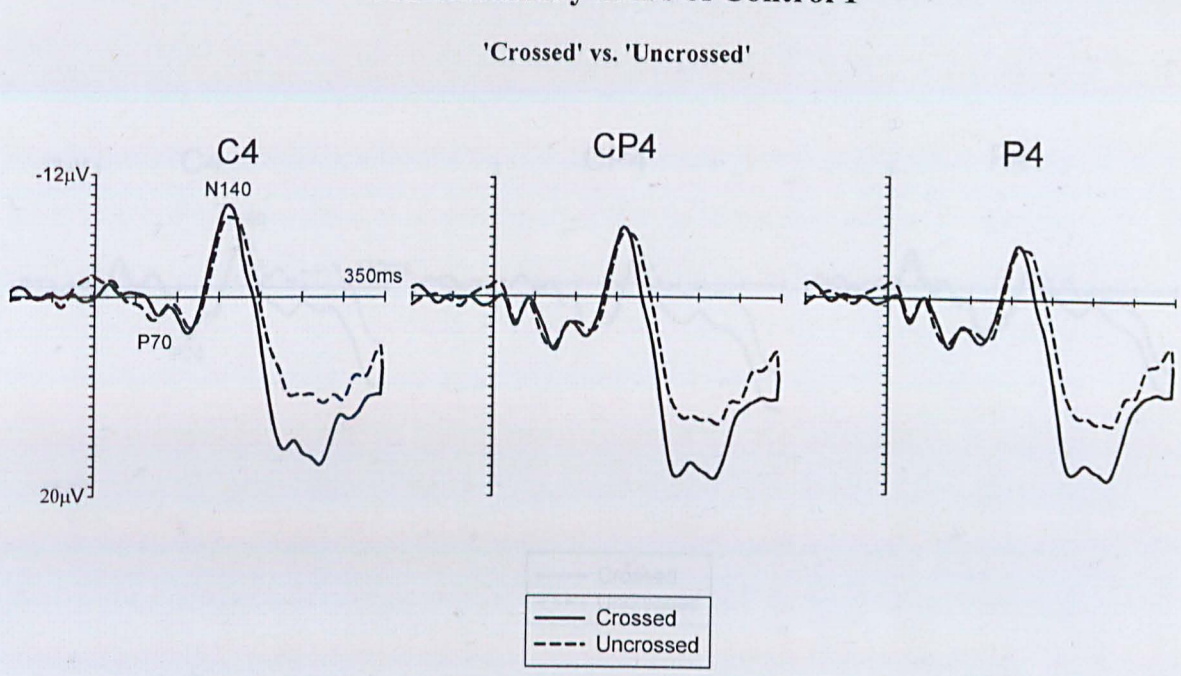


Figure 6.4 Somatosensory ERP waveforms elicited in the 350-ms interval following stimulus onset by tactile stimuli presented to the left hand under crossed (*solid lines*) and uncrossed (*dashed lines*) positions in patient #1. ERPs are displayed for centro-parietal electrodes (C4, CP4, and P4) contralateral to the site of the tactile stimulation (i.e., over the right, damaged, hemisphere).

(a)


Somatosensory ERPs of Control 1
'Crossed' vs. 'Uncrossed'
C4
CP4
P4
-12μV
20μV
N140
P70
350ms
Crossed
Uncrossed

(b)

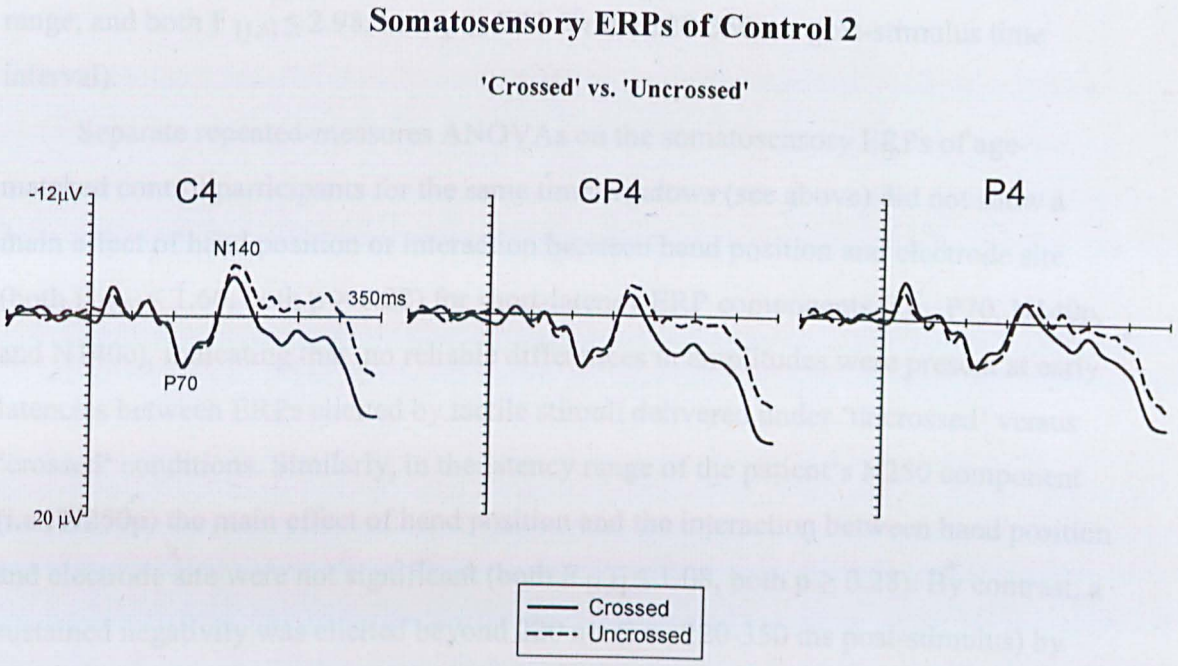


Figure 6.5 Grand-averaged somatosensory ERP waveforms, elicited in the 350-ms interval following stimulus onset by tactile stimuli presented to the left hand under crossed (*solid lines*) and uncrossed (*dashed lines*) positions in two (*a* and *b*) neurologically unimpaired participants. ERPs are displayed for centro-parietal electrodes (C4, CP4, and P4) contralateral to the side of the tactile stimulation (i.e., over the right hemisphere).

Separate repeated-measures analyses of variance on the patient's somatosensory ERPs for the time intervals corresponding to the P70, N140p, N140c, and N250p components (see above), and in the 220-350 post-stimulus interval, with the factors hand position (crossed vs. uncrossed) and electrode site (C4 vs. CP4 vs. P4), revealed a nearly significant effect of hand position in the P70 time interval ($F_{[1,6]} = 5.85$, $p = 0.052$), and a significant effect of this factor in the N140p ($F_{[1,6]} = 6.70$, $p = 0.044$), and in the N250p ($F_{[1,6]} = 9.25$, $p = 0.023$) intervals, reflecting greater amplitudes for ERPs elicited by tactile stimuli under 'crossed' compared to 'uncrossed' conditions. The interaction between hand position and electrode site was not significant for any of the time windows above (all $F_{[1,6]} < 1$, all $p > 0.31$), indicating that the effect of hand position in these time intervals was present for all three electrode sites above and close to somatosensory cortex (see above). In the latency range of the N140c component

(150-195 ms after stimulus onset), and in the subsequent 220-350 ms post-stimulus time interval, the main effect of hand position and the interaction between hand position and electrode site were not significant (both $F_{[1,6]} \leq 2.18$, both $p \geq 0.16$ for the N140c range; and both $F_{[1,6]} \leq 2.98$, both $p \geq 0.13$ for the 220-350 ms post-stimulus time interval).

Separate repeated-measures ANOVAs on the somatosensory ERPs of age-matched control participants for the same time windows (see above) did not show a main effect of hand position or interaction between hand position and electrode site (both $F_{[1,6]} \leq 1.66$, both $p \geq 0.22$) for short-latency ERP components (i.e., P70, N140p, and N140c), indicating that no reliable differences in amplitudes were present at early latencies between ERPs elicited by tactile stimuli delivered under 'uncrossed' versus 'crossed' conditions. Similarly, in the latency range of the patient's N250 component (i.e., N250p) the main effect of hand position and the interaction between hand position and electrode site were not significant (both $F_{[1,6]} \leq 1.08$, both $p \geq 0.28$). By contrast, a sustained negativity was elicited beyond 220 ms (i.e., 220-350 ms post-stimulus) by tactile stimuli delivered under 'uncrossed' compared to 'crossed' hand position, resulting in a main effect of hand position ($F_{[1,6]} = 6.10$, $p < .05$).

6.4 Discussion

All four right-brain-damaged patients were on average faster at responding to tactile stimuli delivered to their left hand when this hand was held in the right, ipsilesional side of space (namely crossed over the bodily midline), compared to when this was held in the contralesional side of space. This finding add to previous observations showing that right-brain-damaged patients are more *accurate* in detecting left-sided tactile stimuli (under conditions of single and double stimulations) when their hands are crossed (Aglioti et al., 1999; Moro et al., 2004; Smania & Aglioti, 1995). These results also add to previous evidence suggesting a crucial role for spatial, not only for sensory, factors in accounting for the somatosensory deficits exhibited by patients with tactile extinction and unilateral spatial neglect (Gallace & Spence, 2007; Moscovitch & Behrmann, 1994; Vallar, 2007; Vallar et al., 1990, 1993, 1997). Processing of tactile (as well as of visual) stimuli by right-brain-damaged patients with extinction to double simultaneous stimulation may be slower for single unilateral stimulation, with increased latencies for stimuli presented in the left-hand side of space,

compared to the right-hand-side, under anatomical (uncrossed) hands posture (Eimer et al., 2002; Marzi, Girelli, Natale, & Miniussi, 2001). A novel finding of the present study is that placing the left hand in the right-hand side of space yields a *temporal advantage* in the processing of tactile stimuli, compared to conditions when that hand is held in the left hand-side of space. This advantage is particularly evident when patients are able to see their stimulated hand. Furthermore, a perusal of the data reveals that in three out of four patients a facilitation of holding the left hand in the right-hand side of space is also present when vision is not available. This pattern of results tallies with a model proposed by Kitazawa (2002) (based on data from neurologically unimpaired participants), which maintains that conscious sensation of touch is localized in space, namely at the location where the stimulated body part lies (in egocentric reference frames), *before* it is localized to the skin (in somatotopic reference frames) (see also Azañón & Soto-Faraco, 2008).

A second novel result is that seeing the left, stimulated hand facilitates tactile detection in right-brain-damaged patients (see also Rorden, Heutink, Greenfield, & Robertson, 1999) by reducing RTs, specifically under crossed hand position. That is, when the left hand was placed in the right, ipsilesional side of space, latencies to tactile stimuli were shorter when patients were able to see their hand compared to when vision was not available. In previous studies that manipulated the position of the hands in order to investigate the role of sensory and spatial reference frames in tactile processing, right-brain-damaged patients (and so the control participants) were blindfolded, as in a standard neurological examination of tactile sensation (Adams et al., 2005). Accordingly, both visual-spatial information and vision of the hand were absent. Because in the present study visual-spatial information was always available (that is, participants kept their eyes open throughout the experiment), our findings specifically suggest that seeing the left hand when placed in the right, ipsilesional side of space further facilitates processing of contralesional tactile stimuli in right-brain-damaged patients. By contrast, vision of the hand does not improve tactile detection when the left hand lies in the left, neglected side of space. In fact, a perusal of the data from the individual patients shows a decrease in performance (i.e., longer response latencies) in patients #1, #2 and #3 when vision was allowed and the left hand was uncrossed. Critically, while patient #1 presented with a left visual field defect, patient #2 had no left hemianopia and patients #3 showed visual extinction to double simultaneous stimulation. In right-brain-damaged patients vision may further bias attentional

resources towards the ipsilesional space, reducing processing efficiency in the contralesional side of space, as also suggested by the findings that spatial neglect is more severe when vision is available (Chokron, Colliot, Bartolomeo, Rhein, Eusop, et al., 2002).

In contrast with the pattern found in right-brain-damaged patients, control participants exhibited a disadvantage when their left hand was crossed over the midline, with their responses being significantly slower under crossed, compared to the anatomical uncrossed, position of the hand. In line with these findings, previous studies in neurologically unimpaired participants show a decrease in performance under crossed hands posture (Shore et al., 2002; Yamamoto & Kitazawa, 2001). In addition, in the controls' group vision of the stimulated hand did not significantly modulate the effect of the spatial position of the hand on tactile detection.

In line with the behavioural results obtained in the patients' group, in one right-brain-damaged patient (#1) moving the left hand towards the right ipsilesional side of space modulated somatosensory processing, as reflected by the enhancement of early ERP components (i.e., P70 and N140), as well as of a longer-latency component (i.e., N250), for left tactile stimuli delivered under conditions when the left hand was crossed over the midline (i.e., in the ipsilesional hemifield) compared to when that hand was placed in an uncrossed position, namely in the contralesional side of space. According to intra-cranial recordings and MEG studies (Allison, McCarthy, & Wood, 1992; Frot & Mauguière, 1999; Hari et al., 1984), somatosensory ERP components elicited within 100 ms, such as the P70, originate within SI, and the somatosensory N140 component originates in SII. The present results therefore suggest that holding the left hand in the 'intact', ipsilesional right-hand-side of space may boost neural activity in the primary somatosensory regions, which, in turn, facilitates detection of tactile stimuli delivered to that hand. In sum, spatial factors, such as the position of the hand, affect sensory cortical responses in patient #1. Previous studies in neurologically unimpaired participants have also shown that spatial attention enhances the amplitude of short-latency somatosensory ERP and MEG components, starting as early as 40-50 ms after stimulus onset (Eimer & Forster, 2003a; Michie et al., 1987; Mima, Nagamine, Nakamura, & Shibasaki, 1998; Schubert et al., 2008). In the present study, the finding that in a right-brain-damaged patient early somatosensory responses are modulated by the spatial position of the stimulated hand is in agreement with the view that the impairment of tactile detection shown by right-brain-damaged patients with left

unilateral visuo-spatial neglect and tactile extinction is due, at least partially, to an impairment of spatial attention, rather than to primary sensory deficits alone (see e.g., Sterzi et al., 1993). This result is also consistent with the finding of a residual activity in the SI and SII regions of the somatosensory cortex of the right hemisphere in patients with tactile extinction, during unilateral left, as well as bilateral, tactile stimulation (see Eimer et al., 2002 for an ERP sudy; and Remy, Zilbovicius, Degos, Bachoud-Lévi, Rancurel, et al., 1999 for a PET study). Such a residual processing may be boosted by the postural shift towards the 'intact' right-hand side of space, allowing a more effective conscious elaboration of the sensory stimulus.

The present finding that the spatial position of the hand can modulate neural responses in early somatosensory areas is also in line with an fMRI study in a right-brain-damaged patient with a mild left unilateral spatial neglect and left tactile extinction. In this study (Valenza, Seghier, Schwartz, Lazeyras, & Vuilleumier, 2004), neural activity in the primary and secondary somatosensory areas was decreased when the patient's right ipsilesional hand was placed in the left (contralesional) side of space, as compared to when the hand was held in the right ipsilesional side of space. Interestingly, fMRI responses were reduced under bilateral as well as unilateral tactile stimulation of the right hand in a crossed position (i.e., in the left-hand side of space). Behaviourally, however, that fMRI study found that the detection of touches to the right hand in a crossed position was dramatically reduced only when a simultaneous stimulation of the right elbow (placed in the right-hand side of space) was given. At the neural level, the results from this study suggest that the spatial position of body parts can modulate the strength of activation of early somatosensory areas also in response to single tactile stimulations, similarly to the results of the present study.

In addition to the modulation of early ERP components, enhancement of the patient's ERPs to tactile stimuli under the crossed, compared to the uncrossed, anatomical position of the left hand was also present at later time intervals (i.e., around 250 ms after onset of the tactile stimuli; corresponding to the somatosensory N250 component). Such long-latency modulations are likely to stem from regions within the premotor frontal-posterior parietal network which are thought to be involved in the control of spatial attention (Corbetta, Miezin, Shulman, & Petersen, 1993; Gitelman, Nobre, Parrish, LaBar, Kim, et al., 1999; Hopfinger, Buonocore, & Mangun, 2000; Mesulam, 1981) and the spatial representation of the body (Serino & Haggard, 2007; Schwoebel & Coslett, 2005; Tsakiris, Hesse, Boy, Haggard, & Fink, 2007). In

agreement with this view, greater activations of the posterior parietal cortex and of the middle frontal gyri were reported in the abovementioned fMRI study (Valenza et al., 2004), when the patient's right hand was held in the ipsilesional side of space (uncrossed position), compared to when that hand was placed in the left, contralesional side of space (crossed position). The increased processing of bodily stimuli through the integration of somatosensory, proprioceptive and visual inputs from the stimulated body part (Maravita et al., 2003; Vallar & Maravita, in press; van Beers et al., 1999) may also contribute to improve the patient's performance when the contralesional hand is crossed over the midline, so that the somatosensory input from that hand is made spatially coincident with the vision of the hand in the ipsilesional, intact visual field. That is, when the stimulated hand lies in the intact hemispace, vision of this hand may aid tactile localization similar to what has been shown by previous studies in healthy participants (Botvinick & Cohen, 1998; Graziano, 1999), which in turn would yield better and faster processing of tactile stimuli.

Unlike in patient #1, early somatosensory components in age-matched controls were not modulated by the spatial position of the left hand. However, a difference between ERPs in response to tactile stimuli emerged at later stages of processing, with a sustained negativity starting from about 220 ms after stimulus onset for stimuli delivered under uncrossed compared to crossed conditions, opposite to the pattern found in the patient. In previous ERP studies performed in healthy participants a sustained negativity was elicited at corresponding latencies by tactile stimuli presented at attended, compared to unattended, locations, indicating facilitation of processing for attended stimuli (Eimer & Forster, 2003a, 2003b; Michie et al., 1987). Our finding that, in neurologically unimpaired participants, tactile stimuli delivered to the left hand in the 'uncrossed' trials elicit an enhanced sustained negativity, compared to the 'crossed' trials, may indicate increased attention allocated to the left hand when this is held in an uncrossed anatomical posture (i.e., when the somatotopic and the spatial frames of reference overlap), compared to when that hand is crossed over the bodily midline.

In sum, the present behavioural and ERP results show that in right-brain-damaged patients with left visuo-spatial neglect and/or tactile extinction moving the left hand to the ipsilesional non-neglected right-hand-side of space may improve somatosensory processing, possibly allocating more attentional resources to the tactile stimuli. In one patient these effects have been shown to start from the very early stages of stimulus processing (namely, in SI and SII), as indexed by an enhancement of early

somatosensory components (P70, N140) under crossed compared to uncrossed posture. These findings may have clinical applications, not only for assessment but also for training to help recovery. Indeed, crossing the hands may help differentiate primary somatosensory deficits from tactile neglect (e.g., Maravita, 2008). Secondly, the rehabilitation of somatosensory neglect may be aided by training the contralesional (left) hand while this lies within the ipsilesional side of space, where the effect of any tactile stimulation may be enhanced.

Chapter 7

Summary and Conclusions

7.1 Introduction

In everyday life, whether we actively interact with objects in our environment or we passively receive a touch on a certain part of our body, we typically gather concurrent tactile and visual information concerning both our body parts (e.g., the hands) and the touched objects. In the past few decades, a converging body of evidence from several approaches (e.g., neurophysiology, neuroimaging, neuropsychology, and psychophysics) has shown that visual and tactile information, typically coming from congruent locations, is integrated at a neural and a perceptual level. In particular, several pieces of evidence have shown that these integrated inputs can modulate unimodal (e.g., tactile) processing (e.g., Kennett et al., 2001b; Làdavas & Farnè, 2004a; Macaluso et al., 2005; Maravita et al., 2002a; Taylor-Clarke et al., 2002). Some of these studies have suggested that the brain represents the body and the space surrounding the body (i.e., peripersonal space) in a *multimodal* fashion, through an integrated visuo-tactile system. However, while single-cell recordings in animals (e.g., Duhamel et al., 1991; Graziano & Gross, 1993, 1995) and neuropsychological studies in humans (Làdavas, 2002; Làdavas, et al., 1998) have provided some evidence supporting the notion that the visuo-tactile representation of peripersonal space may be neurally distinct from the representation of (far) extra-personal space (see Chapter 1 for a review of these studies), research on the neural correlates of crossmodal interactions between vision and touch across space in humans is only at its inception; therefore several issues remain unexplored.

The general aim of the research presented in this thesis was to gain insight on the neural (ERP) correlates of crossmodal representations of the body and of space. The first two studies (Chapters 3 and 4) have addressed whether tactile processing is modulated by crossmodal interactions depending on the relative spatial relationship between tactile stimuli and task-irrelevant visual stimuli when the latter are presented in peripersonal space, in far space, and in 'mirror space'. The other two studies have investigated influences of non-informative vision of the body on tactile spatial

processing; specifically, on spatial attention selection in healthy participants (Chapter 5), and across different hand postures (i.e., crossed vs. uncrossed) in patients with deficits of attention and space representation (Chapters 6). The specific questions addressed and the findings from the studies presented in this thesis will be discussed below, separately for the two visual domains explored: namely, effects of visual stimuli and of vision of the body on tactile processing.

7.2 Crossmodal spatial interactions between task-irrelevant visual stimuli and tactile stimuli

The general purpose of the studies presented in Chapters 3 and 4 was to investigate whether effects of crossmodal visuo-tactile interactions on somatosensory processing (i.e., ERPs recorded over and close to somatosensory cortex) are modulated by spatial congruence between tactile stimuli and task-irrelevant visual stimuli. Previous ERP studies that looked at spatial congruence between vision and touch (Piesco et al., 2005; Schürmann, 2002) compared ERPs elicited by simultaneous bimodal visuo-tactile stimulation with the algebraic sum of ERPs in response to unimodal (i.e., visual and tactile) single stimuli. This method has received some methodological and theoretical criticism (e.g., Gondan & Röder, 2006; Stanford & Stein, 2007; see Chapter 1, sections 1.6 and 1.8). To overcome the limitations of this method, and to specifically investigate whether processing within somatosensory cortex, and response latencies to tactile stimuli, may reflect the strength of crossmodal visuo-tactile interactions depending on the spatial relationship between visual and tactile stimuli, we developed a new crossmodal paradigm whereby visual and tactile stimuli were presented simultaneously in every trial, under different spatial configurations. Thus, only bimodal conditions were compared with each other. In different experimental conditions, task-irrelevant visual stimuli were presented: i) near the hands (i.e., in peripersonal space), either at congruent or incongruent locations as tactile stimuli (in both studies presented in Chapters 3 and 4); ii) at a distance of 70 cm from the participants' hands, either in the same (congruent) or opposite (incongruent) hemispace as tactile stimuli (in the study presented in Chapter 3); and iii) near the participants' covered hands either at congruent or incongruent locations as tactile stimuli, and only visible via a mirror placed at a distance of 35 cm from the participants' hands (in the study presented in Chapter 4). In all experimental conditions, participants were required to attend to either their right or left hand

throughout a block and respond as fast as possible to all tactile target stimuli (stimulation with a 'gap') among tactile non-targets (continuous stimulation) at the attended hand (i.e., tactile discrimination task), while ignoring all visual stimuli.

7.2.1 Peripersonal and far space: ERP evidence for the spatial rule of multisensory interaction

The aim of the study presented in Chapter 3 was to investigate whether crossmodal visuo-tactile interactions modulate behavioural and electrophysiological responses associated with processing within somatosensory cortex depending on the relative spatial location of task-irrelevant visual stimuli with respect to tactile stimuli, when the former are presented in peripersonal and in far space. Although there is a substantial consensus in the literature about the spatial principle of multisensory integration, which maintains that multimodal stimuli presented in close proximity produce enhanced crossmodal effects compared to spatially disparate multimodal stimuli, only a modest number of studies have hitherto investigated the spatial constraints of crossmodal interactions between vision and touch in humans (Forster & Pavone, 2008; Làdavas et al., 1998; Macaluso & Driver, 2005; Piesco et al., 2005; Schürmann et al., 2002; Spence et al., 2004). In these studies, visual stimuli were typically presented in peripersonal space, either at congruent or incongruent locations as touch. Crucially, no neuroimaging or ERP studies have compared visuo-tactile interaction effects when visual stimuli are presented near and far from the body; while single-cell recordings in animals have shown that visuo-tactile integration is more effective for visual stimuli presented within peripersonal space than in far space (see Duhamel et al., 1991; Graziano & Gross, 1993, 1995), and a near-far modulation of crossmodal effects on touch has been reported in the neuropsychological literature (Làdavas et al., 1998). Moreover, the findings from previous ERP studies that have looked at the role of spatial congruence between vision and touch (Piesco et al. 2005; Schürmann et al., 2002) are not consistent, with one study showing greater crossmodal effects (i.e., differences between ERPs in response to bimodal stimulation compared to the sum of unimodal responses) for congruent versus incongruent visuo-tactile stimuli

for some time intervals (Schürmann et al., 2002)[13], and the other (Piesco et al., 2005) failing to find any reliable effect of spatial congruence in crossmodal effects.

The study presented in Chapter 3 aimed to investigate crossmodal visuo-tactile interactions on the radial (near-far), as well as on the horizontal (left-right), dimension; namely, when task-irrelevant visual stimuli were presented in the same (congruent) or opposite (incongruent) hemispace as tactile stimuli, either near the hands (i.e., in peripersonal space) or in far space. The findings from this study are in accordance with the spatial rule of multisensory integration, as demonstrated in the neurophysiological literature (Stein & Meredith, 1993). First, when the visual stimuli were presented in peripersonal space, facilitation in tactile discrimination (i.e., shorter response latencies to tactile target stimuli) and enhanced ERPs recorded over and close to somatosensory cortex were found for congruent compared to incongruent visuo-tactile stimuli. ERP modulations were observed at about 100 ms after onset of stimuli (i.e., overlapping with the P100 component). This finding of crossmodal spatial-congruence effects for visual stimuli presented in peripersonal space adds to previous behavioural, neuroimaging, and neuropsychological evidence (e.g., Làdavas et al., 1998; Macaluso & Driver, 2005; Spence et al., 2004a), and additionally shows that these spatially-specific crossmodal effects occur at early stages of stimuli processing. A second main result of this study is that amplitudes of the P100 component were enhanced and RTs to tactile stimuli were faster when task-irrelevant visual stimuli were presented near the stimulated hand compared to when these were presented in far space. By contrast, response times and ERP amplitudes did not differ significantly between conditions in which visual stimuli were presented in near space at incongruent locations as touch and conditions where visual stimuli were presented in far space. Furthermore, no reliable differences in RTs and ERPs were found when visual stimuli were presented in far space, in the same (congruent) and opposite (incongruent) hemispace as touch. Taken together, these findings indicate that visual stimuli near the stimulated body part are better integrated with tactile stimulation (both at a neural and perceptual level) than visual inputs presented near a different body part or in far space. This would make adaptive and functional sense as in everyday life visual and tactile information typically arises from the same spatial location (e.g., an object in our hand), rather than from disparate sites. If

[13] As outlined in Chapters 1 and 3, in Schurmann et al.'s study (2002) visual stimuli were presented at a distance of one metre from the body (i.e., in far space). Schurmann et al. refer to bimodal conditions in which visual stimuli were presented in the same and opposite hemispace to tactile stimuli as 'congruent' and 'incongruent' conditions, respectively.

spatially-congruent bimodal visual and tactile inputs produce enhanced neural signals compared to spatially non-matching stimuli, then the former are more likely to be combined into a coherent percept. The findings from this study also support previous neurophysiological and neuropsychological studies (Duhamel et al., 1991; Graziano & Gross, 1993; Làdavas et al., 1998), and provide the first neural evidence in humans for an integrated visuo-tactile representation of peripersonal (namely, peri-hand) space, distinct from the representation of far space.

An additional finding of the study presented in Chapter 3 is that tactile-spatial attention modulated ERPs recorded over and near somatosensory cortex independently from and subsequent to crossmodal spatial interactions (i.e., around 140 ms after stimuli onset, N140 component, as well as at later intervals from 200 ms after stimuli onset), with enhanced amplitudes for tactile stimuli presented at attended compared to unattended locations. This finding tallies with a number of previous studies, mainly conducted within the visual and auditory domains, which have suggested that crossmodal interactions occur pre-attentively (e.g., Bertelson et al., 2000; Giard & Peronnet, 1999; Helbig & Ernst, 2008; Vroomen et al., 2001). On the other hand, other evidence supports the view that crossmodal integration and attention may interact (Talsma & Woldorff, 2005; Talsma et al., 2007). It is worth noting that the studies that have reported interaction effects between multimodal processing and attention differ from those that did not find these effects in a number of ways; for example, with respect to the attentional manipulations used (and, possibly, the attentional load); regarding whether both or only one of the two sensory modalities were attended; and whether stimuli were presented centrally or peripherally. While these differences make it difficult to directly compare the findings from these studies, one could speculate that experimental factors may be responsible for the different findings on the interplay between attention and multisensory interactions.

7.2.2 ERP evidence for plasticity of peripersonal space representation

The study presented in Chapter 3 shows that visuo-tactile interactions are more effective in modulating tactile processing when visual stimuli are presented in peripersonal space, specifically when visual and tactile stimuli are spatially congruent. Previous studies have suggested that the visuo-tactile representation of peripersonal space is plastic and, under certain conditions, can include regions of far extra-personal space (Holmes & Spence, 2004; Holmes et al., 2007; Maravita et al., 2000, 2002a,

2002b). For example, behavioural and neuropsychological studies have reported greater crossmodal effects between vision and touch when visual stimuli presented near the hands are indirectly observed in a mirror (i.e., *appearing* in far space) compared to when these *are presented* in far space at a comparable physical distance from the hands (Maravita et al., 2000, 2002a). These findings suggest that mirror-reflected, peripersonal visual stimuli are not treated as far stimuli (i.e., according to their retinal projections), but that they may be remapped as near-the-body stimuli. However, there was no direct evidence for this; and, likewise, no previous studies have investigated whether a remapping of the perceived location of mirror-reflected visual stimuli would occur in an automatic manner or not. The study presented in Chapter 4 aimed to investigate whether crossmodal spatial-congruence effects on somatosensory processing (i.e., stronger crossmodal interactions for spatially congruent compared to incongruent visual and tactile stimuli, as reflected in faster reaction times to tactile stimuli, and enhanced processing within somatosensory cortex; see study presented in Chapter 3) may be obtained when task-irrelevant visual stimuli presented near the hands are viewed as mirror reflections; and, in addition, whether these effects are delayed or not compared to when visual stimuli are viewed directly near the hands.

The results of this study show that under both direct- and mirror-view of the task-irrelevant visual stimuli (and of the participants' own hands) crossmodal interactions are stronger for spatially congruent compared to incongruent visual and tactile stimuli, as indexed by shorter response latencies to tactile stimuli and greater ERPs recorded over and close to somatosensory cortex; suggesting that visual stimuli observed via a mirror may be remapped as peripersonal stimuli. Notably, while in the 'direct-viewing' condition crossmodal spatial-congruence effects were present from 115 ms after onset of visual and tactile stimuli (i.e., overlapping with the N140 component), in the 'mirror-viewing' condition enhancement of ERPs for spatially congruent visuo-tactile stimuli was obtained at later latencies (i.e., from about 190 ms after stimuli onset, overlapping with the N200 component). These crossmodal spatial modulations were present when visual and tactile stimuli were delivered at tactually attended locations but not when these were presented at unattended sites, under both viewing conditions (on the N140 component for the 'direct-viewing' condition, and on the N200 component for the 'mirror-viewing' condition), suggesting an interplay between attention and crossmodal interactions. This result that crossmodal spatial-congruence effects were found to be dependent on the focus of attention is not in line with the finding from the study

presented in Chapter 3, that crossmodal interactions modulated ERPs regardless of whether attention was directed or not to the site of tactile stimulation. As suggested by a brief review of previous relevant work (see Chapter 1, section 1.7), the interplay between attention and crossmodal interactions may depend on experimental factors (e.g., Bertelson et al., 2000; Giard & Peronnet, 1999; Talsma & Woldorff, 2005). In the study presented in Chapter 4, the lighting level of the experimental chamber was greater than in the study presented in Chapter 3, to allow participants to see their hands in the mirror, which as a result caused the visual stimuli to appear less bright. In addition, in the two experimental conditions in which visual stimuli were presented in peripersonal space (i.e., 'near-space' and 'direct-viewing' conditions in Chapters 3 and 4, respectively) participants' gaze direction differed, with the participants' gaze being directed in far space in the study presented in Chapter 3, and in peripersonal space, between the participants' hands, in the other study (see Chapter 4). We could speculate that differences in the lighting level and in gaze direction might alter the relative impact of visual stimuli and of vision of the stimulated body parts (i.e., the hands) on tactile processing, and ultimately affect the interplay between attention and crossmodal integration. The same differences in the abovementioned experimental factors (i.e., lighting level and gaze direction) might be also responsible for the result that in the 'near-space' and 'direct-viewing' conditions crossmodal spatial modulations affected different ERP components (i.e., the P100 and the N140, respectively), although both these components are thought to originate in the same brain areas (i.e., secondary somatosensory areas, SII). However, further investigations would be required to draw more specific conclusions on both these accounts.

Another main result of this study is that crossmodal effects were delayed in the 'mirror-viewing' condition compared to the 'direct-viewing' condition. This delay could be interpreted as evidence that the remapping of mirror-reflected visual stimuli as peripersonal stimuli may require additional time, which in turn may delay crossmodal integration between visual and tactile stimuli by a few tens of milliseconds. In line with this account is the result that in the 'mirror-viewing' condition crossmodal spatial effects on the N200 component were only obtained when stimuli were presented at tactually attended locations (see above). Alternatively, the delay observed for the 'mirror-viewing' condition could be caused by the visual stimuli appearing somewhat dimmer and smaller due to the distance of mirror-reflected lights, and/or by the fact that in this condition the visual stimuli (appearing at a distance from the body) were always

outside the focus of tactile-spatial attention, while in the 'direct-viewing' condition the visual stimuli presented at (tactually) attended locations were within the focus of spatial attention, and therefore they were possibly better processed.

To rule out these potential confounds, a between-subjects analysis was performed to compare ERPs elicited in the 'mirror-viewing' condition (study in Chapter 4) and in the 'far-space' condition, in which visual stimuli were presented at a distance of 70 cm from the participants' hands (study in Chapter 3). These two conditions are comparable for: (a) the distance at which visual stimuli are seen in extra-personal space (i.e, because the mirror was placed half-way between the participants' hands and the location of the "far" visual stimuli, and objects in a mirror are perceived at twice the distance from it); (b) the location of the fixation point (i.e., on the centre of the mirror, and on the centre of a panel covering the mirror, in the 'mirror-viewing' and in the 'far-space' condition, respectively); and (c) the distribution of spatial attention with respect to the location where the visual stimuli appeared (i.e., in extra-personal space).

The results of this analysis showed a significant interaction between the factors 'condition', 'congruence' and 'attention' in the time range of the N200 component, with follow-up tests confirming that crossmodal spatial modulations are only observed when visual stimuli perceived a distance from the body are *known* to originate near the stimulated body part, due to mirror viewing. Moreover, attentional modulations of ERPs did not significantly differ between the 'mirror-viewing' and the 'far-space' conditions, confirming that distribution of spatial attention was similar in these conditions.

Finally, ERPs in the 'mirror-viewing' condition were enhanced compared to the 'far-space' condition in the time interval overlapping with the N200 component and at later latencies, yielding a main effect of condition in these time intervals. It should be noted that the 'mirror-viewing' and the 'far-space' conditions (and so the 'near-space' and the 'far-space' conditions) differ in that the participants' hands are visible near the visual stimuli in the former but not in the latter. Vision of the hands in the 'mirror-viewing' condition might be responsible for the differences between ERPs described above; and, furthermore, it cannot be ruled out that seeing one's own hands next to the visual stimuli may be crucial to produce the crossmodal spatial modulations found in this study. Further investigations should address this issue by having a pair of rubber hands next to the visual stimuli in far space, or by covering the participants' hands in the 'mirror-viewing' condition so that only the visual stimuli would be visible in the mirror.

In addition to the crossmodal effects discussed above, in the main analysis of Chapter 4, we found that in both the 'direct-viewing' and the 'mirror-viewing' conditions tactile-spatial attention modulated ERPs with greater amplitudes for stimuli presented at tactually attended compared to unattended sites in the time range of the N140 and N200 components as well as at later latencies (i.e., from 236 ms after stimuli onset); confirming effects of tactile spatial attention on ERPs found in the study presented in Chapter 3 and in a number of previous studies (e.g., Desmedt & Robertson, 1977; Eimer & Forster, 2003a, 2003b; Michie, 1984; Michie et al., 1987).

7.3 Effects of non-informative vision of the body on tactile processing

In the past decade, increasing evidence has shown that viewing one's own body improves tactile perception and enhances cortical tactile processing (e.g., Fiorio & Haggard, 2005; Kennett et al., 2001b; Press et al., 2004). While it has been argued that this enhancement of touch cannot be attributed to spatial orienting (Fiorio & Haggard, 2005; Kennett et al., 2001b), tactile-spatial attention has also been shown to facilitate responses to touch (e.g., with shorter latencies to tactile stimuli) (see Spence & Gallace, 2007 for a review of behavioural studies), and to enhance brain activity elicited by tactile events (e.g., Eimer & Forster, 2003a, 2003b; Michie et al., 1987). Thus, we could speculate that vision of one's body and attention to a body site may encompass similar purposes (although possibly with distinct mechanisms), namely to enhance the spatial representation of the body part touched, which in turn would facilitate tactile processing. It is therefore plausible to hypothesize that these two processes may work in synergy, and that vision of the body may increase the effects of tactile-spatial attention.

In the study presented in Chapter 5, we directly examined the possibility that vision of the body may specifically aid tactile attentional selection, over ambient visual-spatial information, in healthy participants. The study presented in Chapter 6 investigated whether in right-brain-damaged patients with attentional deficits, vision of the contralesional (left) hand facilitates tactile processing differently when that hand is placed in the patients' left, 'neglected' hemispace (i.e., in an anatomical, uncrossed posture) and when this is crossed over the midline in the right, 'intact' side of space.

7.3.1 Non-informative vision of the body and sustained spatial-tactile attention

The general aim of the study presented in Chapter 5 was to investigate the role of visual information in modulating sustained tactile-spatial attention effects on tactile processing. A previous PET study (Macaluso et al., 2000b) showed that effects of sustained tactile-spatial attention in the intraparietal sulcus (IPS) were enhanced when subjects performed a tactile task with their eyes open as compared to closed, suggesting that ambient visuo-spatial information or vision of the hands (or both) can increase attentional effects on tactile responses. Our study aimed to clarify the latter issue, that is, whether viewing the body or ambient visual information is crucial in modulating attention effects on touch, and to investigate the time course of visual modulations of tactile-spatial attention effects. Participants had to attend to either their right or left hand on each block of stimuli, and to report all tactile target stimuli (stimulation with a 'gap') among tactile non-targets (continuous stimulation) at the currently attended hand as quickly as possible. They performed this tactile discrimination task: (a) under full vision, (b) with their hands covered from view, and (c) blindfolded.

The results of this study show that when both ambient visuo-spatial information and vision of the hands are available (i.e., 'full vision' condition), attentional ERP modulations (i.e., larger amplitudes for attended, compared to unattended, tactile stimuli) are present at earlier stages of somatosensory processing compared to when participants are blindfolded, and, moreover, compared to when participants hands are covered from view. Namely, in the 'full vision' condition (i.e., including vision of the hands) we found attentional modulations of the somatosensory P100 and the N140 components (i.e., about 100 and 140 ms after stimulus onset, respectively), followed by a sustained negativity elicited from about 200 ms post-stimulus onset by tactile stimuli presented at attended, compared to unattended, locations. By contrast, under both 'covered hands' and 'blindfolded' conditions, attentional modulations were not present before 200 ms following stimulus onset, when a sustained negativity was observed for attended, compared to unattended, tactile stimuli. Consistently with this pattern of ERP results, shorter response latencies were found under the 'full vision' condition compared to when participants' hands were covered and when participants were blindfolded.

These results suggest that viewing the body part touched facilitates tactile-spatial selection, as indexed by shorter RTs to tactile stimuli and earlier attentional modulations of somatosensory ERPs. This facilitation by vision of the body may result from independent but converging projections from fronto-parietal brain areas deputed to

attentional control and crossmodal visuo-tactile integration, to somatosensory cortex; or, alternatively, from direct connections between fronto-parietal regions involved in attentional and multisensory processing which would then project back to somatosensory areas. On the other hand, visuo-spatial information per se does not seem to facilitate tactile spatial selection, which suggests that visual modulations of attention effects found in this study are specifically concerned with visual information about the body, not merely about the space around it.

7.3.2 Visual and proprioceptive modulation of tactile extinction

The study presented in Chapter 6 investigated influences of vision and proprioception on tactile processing in right-brain-damaged patients with spatial attention disorders affecting the contralesional side of the space and of the body (i.e., unilateral neglect and/or tactile extinction). Previous studies reported that when right-brain-damaged patients with tactile extinction or neglect crossed their hands over the bodily midline (resulting in their left hand being placed in the right, 'non-neglected' hemispace and vice versa), they were more accurate in reporting tactile stimuli presented to their left contralesional hand for both unilateral single and bilateral double stimuli (Aglioti, et al., 1999; Moscovitch & Behrmann, 1994; Smania & Aglioti, 1995). Notably, in all these studies participants were blindfolded across conditions.

Our study aimed to clarify: first, whether placing the patients' left contralesional hand in the right, 'intact' side of space (i.e., crossed hand position) may specifically improve *processing speed* of unilateral left-sided tactile stimuli, compared to when the patients' left hand is held in the contralesional side of space; second, whether viewing the left, stimulated hand further improves processing speed of tactile stimuli when the patients' hand is placed in the right, ipsilesional hemispace; and, third, whether in right-brain-damaged patients facilitation of tactile detection under crossed, compared to anatomical (uncrossed), hand position is reflected in enhancement of cortical responses to tactile stimuli. To these aims, four right-brain-damaged patients with tactile extinction or neglect, and eight aged-matched neurologically unimpaired control participants were tested in a speeded detection task of unilateral left-sided tactile stimuli when their left hand was either held in uncrossed position or crossed over the midline in the right 'intact' hemispace, either visible or covered from view. In separate sessions, somatosensory ERPs were recorded from one right-brain-damaged patient and two neurologically unimpaired controls in response to unilateral left-sided tactile stimuli

under crossed and uncrossed positions of the left hand, while vision of that hand was always available.

All right-brain-damaged patients showed an overall temporal advantage (i.e., shorter response latencies to tactile stimuli) when their left contralesional hand was placed in the right side of space (i.e., 'crossed' condition) compared to when this was uncrossed in the left side of space; while the performance of the control participants declined when their left hand was crossed over the midline. Moreover, viewing their left hand facilitated performance in right-brain-damaged patients, specifically when that hand was held in the right, non-neglected side of space ('crossed' condition). By contrast, control participants did not show any visual modulation of tactile performance, possibly due to the easiness of the task, in accordance with previous studies in neurologically unimpaired participants (e.g., see Press et al., 2004)

The ERP data in the patient showed enhanced amplitudes for tactile stimuli delivered under the 'crossed' compared to the 'uncrossed' condition, in line with the behavioural results. In particular, this enhancement was observed from early stages of somatosensory processing (i.e., around 70 ms after stimulus onset, overlapping with the somatosensory P70, which is likely to be generated within primary somatosensory cortex, SI; see Hari et al., 1984). The subsequent somatosensory components, namely the N140 and the N250, were also enhanced in the 'crossed' compared to the 'uncrossed' condition. Conversely, the controls' somatosensory ERPs did not show any early modulations by hand position, while a late negativity (starting at around 220 ms after stimulus onset) was present for the 'uncrossed' compared to the 'crossed' hand position; that is, the opposite pattern shown by the patient. In healthy participants, a late negativity is generally elicited by tactile stimuli presented at attended, compared to unattended, body sites (e.g., Eimer et al., 2003a, 2003b; Eimer, Forster, & van Velzen, 2003); suggesting that the late modulation found in the control participants in our study may result from increased attention allocated to the left hand when that hand is held in an anatomical posture, compared to when this is crossed over the bodily midline (that is, when the somatotopic and the externally-anchored reference frames for localizing tactile stimuli are brought into conflict; see, e.g., Shore et al., 2002).

Taken together, these behavioural and ERP results suggest that in right-brain-damaged patients with spatial attention disorders, somatosensory processing may be improved by placing their left contralesional hand in the right 'intact' hemispace; and that patients can further benefit by viewing their left contralesional hand specifically

when that hand is held in the 'non-neglected' side of space. These findings are in accordance with previous literature that maintains that tactile extinction and unilateral neglect are higher-order spatial and attentional, rather than purely sensory, disorders (see, e.g., Vallar, 1998).

7.4 Conclusions and directions for future research

The studies presented in this thesis contribute to the field of multisensory integration with novel behavioural and neural (ERP) findings. New evidence has been provided showing that crossmodal integration between task-irrelevant visual stimuli and tactile stimuli is most effective when multisensory stimuli are spatially congruent, including when spatial congruence is inferred rather than real (i.e., when visual stimuli are indirectly observed in a mirror) (Chapters 3 and 4). Additional investigations could further elucidate whether visuo-tactile spatial-congruence effects on ERPs reflect a spread of activation within the hemisphere to which the visual and tactile stimuli are initially projected (i.e., contralateral to the side of stimulation), or rather these depend on spatial congruence between visual and tactile stimuli in external spatial coordinates irrespective of the initial hemispheric projections of stimuli. A similar issue has been investigated in previous behavioural and ERP studies with respect to crossmodal links in spatial attention when visual and tactile stimuli are not simultaneously presented (Eimer et al., 2001; Kennett et al., 2002). The results from these studies show that, when participants' hands are crossed over the bodily midline so that the right hand lies in the left hemispace and vice versa, visuo-tactile links in spatial attention are stronger for visual and tactile stimuli presented at congruent locations in external space (e.g., when the visual stimuli are presented in the right hemispace and the tactile stimuli to the left hand, which lies in the right hemispace) compared to when visual and tactile stimuli are presented at opposite locations in external space and initially project to the same hemisphere (e.g. when the visual stimuli are presented in the right hemispace and the tactile stimuli to the right hand, which is placed in the left hemispace). The paradigm that we used in the studies described in Chapters 3 and 4 could be adapted in a similar way (i.e., with the participants performing the task under crossed- and uncrossed-hands postures) to test whether spatial-congruence effects between *simultaneously* presented visual and tactile stimuli rely on 'hemispheric activations' (see Eimer et al., 2001), or rather on crossmodal stimuli being presented at congruent locations in external space.

Another interesting line of enquiry would be to establish whether visuo-tactile spatial-congruence effects require that participants' hands are visible along with the visual stimuli, particularly in the 'mirror viewing' condition (see Chapter 4). A number of neurophysiological and neuropsychological studies have shown that seeing the stimulated hand is crucial for integrating tactile inputs and visual stimuli presented in peripersonal space (Graziano et al., 1994; Làdavas et al., 2000; MacKay & Crammon, 1987). On the other hand, there are examples of visuo-tactile effects (namely, crossmodal links in exogenous spatial attention whereby visual and tactile stimuli are not concurrently presented) that have been reported under conditions when the participants' hands are unseen (see Kennett et al., 2002). If in the mirror-viewing condition crossmodal spatial-congruence effects on ERPs were found when the participants' hands are visible but these crossmodal effects were reduced or absent when the participants' hands are covered from view, this would suggest that the remapping of mirror-reflected visual stimuli as peripersonal stimuli is specifically triggered by seeing the mirror reflection of one's own hands and the space around them, rather than by the knowledge of the properties of mirror-reflecting surfaces alone (see Chapter 4). Alternatively, if these crossmodal effects were also found under 'unseen-hands' conditions, that might suggest a greater role for higher level processes in the spatial remapping of visual stimuli.

Finally, the studies presented in this thesis have also shown that viewing one's own body aids tactile spatial processing in healthy individuals and in patients with spatial attention disorders (Chapters 5 and 6). In the context of the findings from these studies, it would be interesting to explore further the role of vision of the body on the 'crossed-hand' effect in right-brain-damaged patients with tactile neglect or extinction, by investigating whether in these patients viewing their contralesional hand in a mirror under crossed and uncrossed postures produce similar effects as those observed under direct vision of the hand (see Chapter 6). This paradigm could be used to investigate somatosensory and attentional deficits in right-brain-damaged patients with tactile neglect and/or extinction and associated somatoparaphrenia, specifically delusion of disownership of contralesional body parts (see Vallar & Ronchi, 2009 for a recent review on somatoparaphrenia). Moro et al. (2004) reported that in two right-brain-damaged patients with somatoparaphrenia, changing the spatial position of the left contralesional hand towards the right non-neglected hemispace (i.e., crossed hand position) reduced tactile extinction while it did not affect disownership of the

contralesional hand. As exposure to mirrors has been shown to either correct (Assal, 1983; Verret & Lapresle, 1978) or induce (Paysan, Beis, Le Chapelain, & André, 2004) delusion of disownership in somatoparaphrenic patients, the use of a mirror within the "crossed-hand" task might further improve or, instead, deteriorate tactile perception in neglect/extinction patients with somatoparaphrenia, by respectively increasing or decreasing their feeling of ownership of the contralesional hand. The outcome of this investigation could shed light on the extent to which unilateral neglect and delusion of disownership of contralesional body parts are dissociated in right-brain-damaged patients (see Moro et al., 2004; see also Vallar & Ronchi, 2009).

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